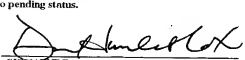


M10 Rec'd PCT/PTO 18 JAN 2002

FORM PTO-3700 OFFICE		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK	ATTORNEY'S DOCKET NUMBER PF-0722 USN
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371			U.S. APPLICATION NO. (If known, see 37 CFR 1.5) TO BE ASSIGNED 10/031915
INTERNATIONAL APPLICATION NO. PCT/US00/19948	INTERNATIONAL FILING DATE 21 July 2000	PRIORITY DATE CLAIMED 21 July 1999	
TITLE OF INVENTION CELL CYCLE AND PROLIFERATION PROTEINS			
APPLICANT(S) FOR DO/EO/US HILLMAN, Jennifer; LAL, Preeti; TANG, Y. Tom; YUE, Henry; AU-YOUNG, Janice; BANDMAN, Olga; AZIMZAI, Yalda; YANG, Junming; LU, Dyung Anna M.; BAUGHN, Mariah R.; PATTERSON, Chandra; SHAH, Purvi			
<p>Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:</p> <ol style="list-style-type: none"> <input checked="" type="checkbox"/> This is the FIRST submission of items concerning a filing under 35 U.S.C. 371. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. <input type="checkbox"/> This is an express request to promptly begin national examination procedures (35 U.S.C. 371 (f)). <input type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (PCT Article 31). <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) <ol style="list-style-type: none"> <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau) <input type="checkbox"/> has been communicated by the International Bureau. <input checked="" type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) <ol style="list-style-type: none"> <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). <input type="checkbox"/> have been communicated by the International Bureau. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. <input type="checkbox"/> have not been made and will not be made. <input checked="" type="checkbox"/> attached hereto Article 34 Amendment <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). 			
<p>Items 11 to 16 below concern document(s) or information included:</p> <ol style="list-style-type: none"> <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.27 and 3.31 is included. <input checked="" type="checkbox"/> A FIRST preliminary amendment, as follows: Cancel in this application original claims #12, 14, 18, 20, 21, 23, 24, 27 before calculating the filing fee, without prejudice or disclaimer. Applicants submit that these claims were included in the application as filed in the interest of providing notice to the public of certain specific subject matter intended to be claimed, and are being canceled at this time in the interest of reducing filing costs. Applicants expressly state that these claims are not being canceled for reasons related to patentability, and are in fact fully supported by the specification as filed. Applicants expressly reserve the right to reinstate these claims or to add other claims during prosecution of this application or a continuation or divisional application. Applicants expressly do not disclaim the subject matter of any invention disclosed herein which is not set forth in the instantly filed claims. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. <input type="checkbox"/> A substitute specification. <input type="checkbox"/> A change of power of attorney and/or address letter. <input checked="" type="checkbox"/> Other items or information: 1) Transmittal Letter (2 pp, in duplicate) 2) Return Postcard 3) Express Mail Label No.: EL 856149 089 US 4) Sequence Listing Statement and Diskette 5) Article 34 Amendment 			

JC13 Rec'd PCT/PTO 18 JAN 2002

U.S. APPLICATION NO. (if known, see 37 CFR 1.5) 10/031915 TO BE ASSIGNED		INTERNATIONAL APPLICATION NO. PCT/US00/19948	ATTORNEY'S DOCKET NUMBER PF-0722 USN
17. 8 The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)): Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO.....\$1000.00 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO.....\$860.00 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO.....\$710.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4).....\$690.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4).....\$100.00			
ENTER APPROPRIATE BASIC FEE AMOUNT =			\$710.00
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).			\$
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE
Total Claims	20 =	0	X \$ 18.00
Independent Claims	3 =	0	X \$ 80.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$270.00
TOTAL OF ABOVE CALCULATIONS =			\$
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.			\$
= SUBTOTAL			\$710.00
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).			\$
TOTAL NATIONAL FEE =			\$710.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by the appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property			+
TOTAL FEES ENCLOSED =			\$710.00
			Amount to be Refunded: \$
			Charged: \$
a. <input type="checkbox"/> A check in the amount of \$ _____ to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. <u>09-0108</u> in the amount of \$710.00 _____ to cover the above fees. c. <input type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>09-0108</u> . A duplicate copy of this sheet is enclosed.			
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.			
SEND ALL CORRESPONDENCE TO:			
INCYTE GENOMICS, INC. 3160 Porter Drive Palo Alto, CA 94304			
SIGNATURE:  NAME: Diana Hamlet-Cox			
REGISTRATION NUMBER: 33,302			
DATE: <u>18 January 2002</u>			

"Express Mail" mailing label number EL 892 011 785 US. I hereby certify that this document and referenced attachments are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR § 1.10 on the date indicated and is addressed to: Commissioner for Patents, Box PCT, USPTO, P.O. Box 2327 Arlington, Virginia 22207 on 12-6-01.

By: *Nancy Ramos*Printed: Nancy RamosCHAPTER II

INTERNATIONAL EXAMINING AUTHORITY (IPEA/US)

PCT/US00/19948

21 July 2000

21 July 1999

INTERNATIONAL APPLICATION NO.

INTERNATIONAL FILING DATE

PRIORITY DATE CLAIMED

CELL CYCLE AND PROLIFERATION PROTEINS

TITLE OF INVENTION

INCYTE GENOMICS, INC.

APPLICANT

United States Patent and Trademark Office

P.O. Box PCT

Washington, D.C. 20231

EL892011785US

ARTICLE 34 AMENDMENT

Dear Sirs:

Please add new claims 29-192 in the above referenced international application as indicated below. A clean copy of the affected claims is attached (see pages 111/1-111/15). The replacement pages represent the new claims to be added as well as replacement page 111/1. These new claims do not go beyond the disclosure as filed.

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: 05 Dec 2001*Diana Hamlet-Cox*
Diana Hamlet-Cox, Ph.D., Esq.

Reg. No. 33,302

Direct Dial Telephone: (650) 845-4639

Date: 24 Dec 2001*Michelle M. Stempien*
Michelle M. Stempien

Reg. No. 41,327

Direct Dial Telephone (650) 843-7219

with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.

5 27. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

- a) exposing a sample comprising the target polynucleotide to a compound, and
- b) detecting altered expression of the target polynucleotide.

10

28. A method for assessing toxicity of a test compound, said method comprising:

- a) treating a biological sample containing nucleic acids with the test compound;
- b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at

least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific

15 hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 11 or fragment thereof;

- c) quantifying the amount of hybridization complex; and

20 d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

25 29. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

- a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,

- b) detecting altered expression of the target polynucleotide, and

30 c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

30. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:1.

35 31. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:2.

32. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:3.
33. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:4.
34. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:5.
35. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:6.
36. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:7.
37. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:10.
38. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:11.
39. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:12.
40. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:13.
41. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:14.
42. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:15.
43. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:17.
44. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:18.
45. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:20.
46. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:22.
47. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:23.
48. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:24.
49. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:25.

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50. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:26.

51. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:28.

52. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:29.

53. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:30.

54. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:31.

55. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:32.

56. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:33.

57. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:34.

58. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:35.

59. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:36.

60. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:37.

61. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:38.

62. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:39.

63. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:41.

64. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:42.

65. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:43.

66. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:44.

67. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:45.

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68. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:46.

69. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:47.

70. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:48.

71. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:50.

72. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:51.

73. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:52.

74. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:53.

75. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:54.

76. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:55.

77. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:56.

78. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:57.

79. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:58.

80. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:59.

81. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:60.

82. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:61.

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83. A polynucleotide of claim 11, comprising the polynucleotide

NO:64.

84. A polynucleotide of claim 11, comprising the polynucleot

NO:65.

85. A polynucleotide of claim 11, comprising the polynucleotide sequence

NO:66.

86. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID

NO:67.

87. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID

NO:68.

88. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID

NO:69.

89. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID

NO:71.

90. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID

NO:72.

91. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID

NO:74.

92. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID

NO:76.

93. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID

NO:77.

94. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID

NO:78.

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95. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:79.

96. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:80.

97. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:82.

98. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:83.

99. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:84.

100. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:85.

101. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:86.

102. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:87.

103. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:88.

104. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:89.

105. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:90.

106. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:91.

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107. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:92.

108. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:93.

109. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:95.

110. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:96.

111. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:97.

112. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:98.

113. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:99.

114. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:100.

115. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:101.

116. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:102.

117. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:104.

118. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID
NO:105.

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119. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:106.
120. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:107.
121. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:108.
122. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:1.
123. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:2.
124. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:3.
125. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:4.
126. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:5.
127. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:6.
128. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:7.
129. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:10.
130. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:11.
131. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:12.
132. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:13.
133. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:14.
134. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:15.
135. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:17.

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136. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:18.

137. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:20.

5 138. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:22.

139. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:23.

140. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:24.

10

141. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:25.

142. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:26.

15 143. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:28.

144. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:29.

145. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:30.

20

146. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:31.

147. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:32.

25 148. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:33.

149. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:34.

150. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:35.

30

151. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:36.

152. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:37.

35 153. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:38.

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154. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:39.

155. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:41.

5 156. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:42.

157. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:43.

158. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:44.

10 159. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:45.

160. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:46.

15 161. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:47.

162. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:48.

163. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:50.

20 164. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:51.

165. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:52.

25 166. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:53.

167. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:54.

30 168. A diagnostic test for a condition or disease associated with the expression of human cell cycle and proliferation proteins (CCYPR) in a biological sample comprising the steps of:

- a) combining the biological sample with an antibody of claim 10, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex; and
- b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.

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169. The antibody of claim 10, wherein the antibody is:

- a) a chimeric antibody,
- b) a single chain antibody,
- c) a Fab fragment,
- 5 d) a F(ab')₂ fragment, or
- e) a humanized antibody.

170. A composition comprising an antibody of claim 10 and an acceptable excipient.

10 171. A method of diagnosing a condition or disease associated with the expression of human cell cycle and proliferation proteins (CCYPR) in a subject, comprising administering to said subject an effective amount of the composition of claim 170.

172. A composition of claim 170, wherein the antibody is labeled.

15

173. A method of diagnosing a condition or disease associated with the expression of human cell cycle and proliferation proteins (CCYPR) in a subject, comprising administering to said subject an effective amount of the composition of claim 172.

20

174. A method of preparing a polyclonal antibody with the specificity of the antibody of claim 10 comprising:

- a) immunizing an animal with a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:11,
 - 25 SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ ID NO:54, or an immunogenic fragment thereof, under conditions to elicit an antibody response;
- b) isolating antibodies from said animal; and
- 35 c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having an amino acid

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SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5,
 SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:11, SEQ ID
 NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17,
 SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID
 NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
 SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID
 NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38,
 SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID
 NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48,
 SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ
 ID NO:54.

178. A monoclonal antibody produced by a method of claim 177.

179. A composition comprising the antibody of claim 178 and a suitable carrier.

180. The antibody of claim 10, wherein the antibody is produced by screening a Fab expression library.

181. The antibody of claim 10, wherein the antibody is produced by screening a recombinant immunoglobulin library.

182. A method for detecting a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ ID NO:54, in a sample comprising the steps of:

- a) incubating the antibody of claim 10 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and
- b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide having an amino acid sequence selected from the group consisting of

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184. A microarray wherein at least one element of the microarray is a polynucleotide of claim 12.

185. A method for generating a transcript image of a sample which contains polynucleotides, the method comprising the steps of:

- a) labeling the polynucleotides of the sample,
- b) contacting the elements of the microarray of claim 184 with the labeled polynucleotides of the sample under conditions suitable for the formation of a hybridization complex, and
- c) quantifying the expression of the polynucleotides in the sample.

186. An array comprising different nucleotide molecules affixed in distinct physical locations on a solid substrate, wherein at least one of said nucleotide molecules comprises a first oligonucleotide or polynucleotide sequence specifically hybridizable with at least 30 contiguous nucleotides of a target polynucleotide, said target polynucleotide having a sequence of claim 11.

187. An array of claim 186, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 30 contiguous nucleotides of said target polynucleotide.

188. An array of claim 186, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 60 contiguous nucleotides of said target polynucleotide.

189. An array of claim 186, which is a microarray.

190. An array of claim 186, further comprising said target polynucleotide hybridized to said first oligonucleotide or polynucleotide.

191. An array of claim 186, wherein a linker joins at least one of said nucleotide molecules to said solid substrate.

192. An array of claim 186, wherein each distinct physical location on the substrate contains multiple nucleotide molecules having the same sequence, and each distinct physical location on the substrate contains nucleotide molecules having a sequence which differs from the sequence of nucleotide molecules at another physical location on the substrate.

CELL CYCLE AND PROLIFERATION PROTEINS

TECHNICAL FIELD

This invention relates to nucleic acid and amino acid sequences of cell cycle and proliferation
5 proteins and to the use of these sequences in the diagnosis, treatment, and prevention of immune,
developmental, and cell signaling disorders, and cell proliferative disorders including cancer.

BACKGROUND OF THE INVENTION

Cell division is the fundamental process by which all living things grow and reproduce. In
10 unicellular organisms such as yeast and bacteria, each cell division doubles the number of organisms,
while in multicellular species many rounds of cell division are required to replace cells lost by wear or
by programmed cell death, and for cell differentiation to produce a new tissue or organ. Details of the
cell division cycle may vary, but the basic process consists of three principal events. The first event,
15 interphase, involves preparations for cell division, replication of the DNA, and production of essential
proteins. In the second event, mitosis, the nuclear material is divided and separates to opposite sides of
the cell. The final event, cytokinesis, is division and fission of the cell cytoplasm. The sequence and
timing of cell cycle transitions are under the control of the cell cycle regulation system which controls
the process by positive or negative regulatory circuits at various check points.

Mitosis marks the end of interphase and concludes with the onset of cytokinesis. There are four
20 stages in mitosis, occurring in the following order: prophase, metaphase, anaphase and telophase.
Prophase includes the formation of bi-polar mitotic spindles, composed of microtubules and associated
proteins such as dynein, which originate from polar mitotic centers. During metaphase, the nuclear
material condenses and develops kinetochore fibers which aid in its physical attachment to the mitotic
spindles. The ensuing movement of the nuclear material to opposite poles along the mitotic spindles
25 occurs during anaphase. Telophase includes the disappearance of the mitotic spindles and kinetochore
fibers from the nuclear material. Mitosis depends on the interaction of numerous proteins. For
example, mutation studies in the *Drosophila melanogaster zw10* gene show a disruption in chromosome
segregation. ZW10 protein appears to function at the kinetochore as a tension-sensing checkpoint
during the onset of anaphase. ZW10 appears to have a direct role in the recruitment of dynein to the
30 kinetochore, and, dynein's involvement in the coordination of chromosome separation at the onset of
anaphase and/or poleward movement (Starr, D.A. et al. (1998) *J. Cell Biol.* 142:763-774).

Regulated progression of the cell cycle depends on the integration of growth control pathways
with the basic cell cycle machinery. Cell cycle regulators have been identified by selecting for human
and yeast cDNAs that block or activate cell cycle arrest signals in the yeast mating pheromone pathway

when they are overexpressed. Known regulators include human CPR (cell cycle progression restoration) genes, such as CPR8 and CPR2, and yeast CDC (cell division control) genes, including CDC91, that block the arrest signals. The CPR genes express a variety of proteins including cyclins, tumor suppressor binding proteins, chaperones, transcription factors, translation factors, and

- 5 RNA-binding proteins (Edwards, M.C. et al. (1997) Genetics 147:1063-1076).

- The human CDC protein, CDC23, is homologous to the S. cerevisiae protein CDC23 which functions in the transition from metaphase to anaphase as well as in the exit from mitosis (Zhao, N. et al. (1998) Genomics 53:184-190). The C. elegans gene cullin-1 (cull1) is a negative regulator of the cell cycle. cull1 regulates the G1 to S phase transition and C. elegans cull1 mutants exhibit hyperplasia of all
10 tissues through acceleration of this transition by overriding mitotic arrest. cull1 is a member of a conserved gene family that spans S. cerevisiae, nematodes and humans (Kipreos, E.T. et al. (1996) Cell 85:929-939).

- Several cell cycle transitions, including the entry and exit of a cell from mitosis, are dependent upon the activation and inhibition of cyclin-dependent kinases (Cdks). The Cdks are composed of a
15 kinase subunit, Cdk, and an activating subunit, cyclin, in a complex that is subject to many levels of regulation. There appears to be a single Cdk in Saccharomyces cerevisiae and Schizosaccharomyces pombe whereas mammals have a variety of specialized Cdks. Cyclins act by binding to and activating cyclin-dependent protein kinases which then phosphorylate and activate selected proteins involved in the mitotic process. The Cdk-cyclin complex is both positively and negatively regulated by
20 phosphorylation, and by targeted degradation involving molecules such as CDC4 and CDC53. In addition, Cdks are further regulated by binding to inhibitors and other proteins such as Suc1 that modify their specificity or accessibility to regulators (Patra, D. and W.G. Dunphy (1996) Genes Dev. 10:1503-1515; and Mathias, N. et al. (1996) Mol. Cell Biol. 16:6634-6643).

Reproduction

- 25 The male and female reproductive systems are complex and involve many aspects of growth and development. The anatomy and physiology of the male and female reproductive systems are reviewed in Guyton, A.C. ((1991) Textbook of Medical Physiology, W.B. Saunders Co., Philadelphia PA, pp.899-928).

- The male reproductive system includes the process of spermatogenesis, in which the sperm are
30 formed. Male reproductive functions are regulated by various hormones. The hormones exert their effects on accessory sexual organs, and are involved in cellular metabolism, growth, and other bodily functions.

Spermatogenesis begins at puberty as a result of stimulation by gonadotropic hormones released from the anterior pituitary. Immature sperm (spermatogonia) undergo several mitotic cell

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divisions before undergoing meiosis and full maturation. The testes secrete several male sex hormones. Testosterone, the most abundant, is essential for growth and division of the immature sperm, and for the masculine characteristics of the male body. Three other male sex hormones, gonadotropin-releasing hormone (GnRH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH), control sexual function.

The uterus, ovaries, fallopian tubes, vagina, and breasts comprise the female reproductive system. The ovaries and uterus are the source of ova and the location of fetal development, respectively. The fallopian tubes and vagina are accessory organs attached to the top and bottom of the uterus, respectively. Both the uterus and ovaries have additional roles in the development and loss of reproductive capability during a female's lifetime. The primary role of the breasts is lactation. Multiple endocrine signals from the ovaries, uterus, pituitary, hypothalamus, adrenal glands, and other tissues coordinate reproduction and lactation. These signals vary during the monthly menstruation cycle and during the female's lifetime. Similarly, the sensitivity of reproductive organs to these endocrine signals varies during the female's lifetime.

A combination of positive and negative feedback to the ovaries, pituitary and hypothalamus glands controls physiologic changes during the monthly ovulation and endometrial cycles. The anterior pituitary secretes two major gonadotropin hormones, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), regulated by negative feedback of steroids, most notably by ovarian estradiol. If fertilization does not occur, estrogen and progesterone levels decrease. This sudden reduction of the ovarian hormones leads to menstruation, the desquamation of the endometrium.

Hormones further govern all the steps of pregnancy, parturition, lactation, and menopause. During pregnancy large quantities of human chorionic gonadotropin (hCG), estrogens, progesterone, and human chorionic somatomammotropin (hCS) are formed by the placenta. hCG, a glycoprotein similar to luteinizing hormone, stimulates the corpus luteum to continue producing more progesterone and estrogens, rather than to involute as occurs if the ovum is not fertilized. hCS is similar to growth hormone and is crucial for fetal nutrition.

The female breast also matures during pregnancy. Large amounts of estrogen secreted by the placenta trigger growth and branching of the breast milk ductal system while lactation is initiated by the secretion of prolactin by the pituitary gland.

Parturition involves several hormonal changes that increase uterine contractility toward the end of pregnancy, as follows. The levels of estrogens increase more than those of progesterone. Oxytocin is secreted by the neurohypophysis. Concomitantly, uterine sensitivity to oxytocin increases. The fetus itself secretes oxytocin, cortisol (from adrenal glands), and prostaglandins.

Menopause occurs when most of the ovarian follicles have degenerated. The ovary then

produces less estradiol, reducing the negative feedback on the pituitary and hypothalamus glands. Mean levels of circulating FSH and LH increase, even as ovulatory cycles continue. Therefore, the ovary is less responsive to gonadotropins, and there is an increase in the time between menstrual cycles. Consequently, menstrual bleeding ceases, and reproductive capability ends.

5 Differentiation and Proliferation

Tissue growth involves complex and ordered patterns of cell proliferation, cell differentiation, and apoptosis. Cell proliferation must be regulated to maintain both the number of cells and their spatial organization. This regulation depends upon the appropriate expression of proteins which control cell cycle progression in response to extracellular signals, such as growth factors and other mitogens, and intracellular cues, such as DNA damage or nutrient starvation. Molecules which directly or indirectly modulate cell cycle progression fall into several categories, including growth factors and their receptors, second messenger and signal transduction proteins, oncogene products, tumor-suppressor proteins, and mitosis-promoting factors.

Embryogenesis is a process in which distinct patterns of protein expression control proper development. This process involves a host of proteins each with distinct and highly coordinated expression patterns. For example, in the mouse, temporally regulated expression of two related genes *Msg1* and *Mrg1* contribute to normal embryonic development. *Msg1* is expressed in the posterior domains of the developing mesoderm, while *Mrg1* is expressed in the anterior visceral endoderm. Properly coordinated expression of each protein throughout embryogenesis is critical for proper tissue and organ formation (Dunwoodie, S.L. et al. (1998) *Mech. Dev.* 72:27-40).

Growth factors were originally described as serum factors required to promote cell proliferation. Most growth factors are large, secreted polypeptides that act on cells in their local environment. Growth factors bind to and activate specific cell surface receptors and initiate intracellular signal transduction cascades. Many growth factor receptors are classified as receptor tyrosine kinases which undergo autophosphorylation upon ligand binding. Autophosphorylation enables the receptor to interact with signal transduction proteins characterized by the presence of SH2 or SH3 domains (Src homology regions 2 or 3). These proteins then modulate the activity state of small G-proteins, such as Ras, Rab, and Rho, along with GTPase activating proteins (GAPs), guanine nucleotide releasing proteins (GNRPs), and other guanine nucleotide exchange factors. Small G proteins act as molecular switches that activate other downstream events, such as mitogen-activated protein kinase (MAP kinase) cascades. MAP kinases ultimately activate transcription of mitosis-promoting genes.

In addition to growth factors, small signaling peptides and hormones also influence cell proliferation. These molecules bind primarily to another class of receptor, the trimeric G-protein

coupled receptor (GPCR), found predominantly on the surface of immune, neuronal and neuroendocrine cells. Upon ligand binding, the GPCR activates a trimeric G protein which in turn triggers increased levels of intracellular second messengers such as phospholipase C, Ca^{2+} , and cyclic AMP. Most GPCR-mediated signaling pathways indirectly promote cell proliferation by causing the secretion or
5 breakdown of other signaling molecules that have direct mitogenic effects. These signaling cascades often involve activation of kinases and phosphatases. Some growth factors, such as some members of the transforming growth factor beta (TGF- β) family, act on some cells to stimulate cell proliferation and on other cells to inhibit it. Growth factors may also stimulate a cell at one concentration and inhibit the same cell at another concentration. Most growth factors also have a multitude of other actions
10 besides the regulation of cell growth and division; they can control the proliferation, survival, differentiation, migration, or function of cells depending on the circumstance. For example, the tumor necrosis factor/nerve growth factor (TNF/NGF) family can activate or inhibit cell death, as well as regulate proliferation and differentiation. The cell response depends on the type of cell, its stage of differentiation and transformation status, which surface receptors are stimulated, and the types of
15 stimuli acting on the cell (Smith, A. et al. (1994) Cell 76:959-962; and Nocentini, G. et al. (1997) Proc. Natl. Acad. Sci. USA 94:6216-6221).

Neighboring cells in a tissue compete for growth factors, and when provided with "unlimited" quantities in a perfused system will grow to even higher cell densities before reaching density-dependent inhibition of cell division. Cells often demonstrate an anchorage dependence of cell division as well.
20 This anchorage dependence may be associated with the formation of focal contacts linking the cytoskeleton with the extracellular matrix (ECM). The expression of ECM components can be stimulated by growth factors. For example, TGF- β stimulates fibroblasts to produce a variety of ECM proteins, including fibronectin, collagen, and tenascin (Pearson, C.A. et al. (1988) EMBO J. 7:2977-2981). In fact, for some cell types, specific ECM molecules, such as laminin or fibronectin, may act as
25 growth factors. Tenascin-C and -R, expressed in developing and lesioned neural tissue, provide stimulatory/anti-adhesive or inhibitory properties, respectively, for axonal growth (Faissner, A. (1997) Cell Tissue Res. 290:331-341).

Cancers and immune disorders are characterized by uncoordinated cell proliferation. Cancers are associated with the activation of oncogenes which are derived from normal cellular genes. These
30 oncogenes encode oncoproteins which convert normal cells into malignant cells. Some oncoproteins are mutant isoforms of the normal protein, and other oncoproteins are abnormally expressed with respect to location or amount of expression. The latter category of oncoprotein causes cancer by altering transcriptional control of cell proliferation. Five classes of oncoproteins are known to affect cell cycle controls. These classes include growth factors, growth factor receptors, intracellular signal

transducers, nuclear transcription factors, and cell-cycle control proteins. Viral oncogenes are integrated into the human genome after infection of human cells by certain viruses. Examples of viral oncogenes include v-src, v-abl, and v-fps. Certain cell proliferation disorders can be identified by changes in the protein complexes that normally control progression through the cell cycle. A primary treatment strategy involves reestablishing control over cell cycle progression by manipulation of the proteins involved in cell cycle regulation (Nigg, E.A. (1995) BioEssays 17:471-480).

Many oncogenes have been identified and characterized. These include sis, erbA, erbB, her-2, mutated Gs, src, abl, ras, crk, jun, fos, myc, and mutated tumor-suppressor genes such as RB, p53, mdm2, Cip1, p16, and cyclin D. Transformation of normal genes to oncogenes may also occur by chromosomal translocation. The Philadelphia chromosome, characteristic of chronic myeloid leukemia and a subset of acute lymphoblastic leukemias, results from a reciprocal translocation between chromosomes 9 and 22 that moves a truncated portion of the proto-oncogene c-abl to the breakpoint cluster region (bcr) on chromosome 22.

Mutations which hyperactivate oncogenes result in cell proliferation. Stimulation of a cell by growth factors activates two sets of gene products, the early-response genes and the delayed-response genes. Early-response gene products include myc, fos, and jun, all of which encode gene regulatory proteins. These regulatory proteins lead to the transcriptional activation of a second set of genes, the delayed-response genes, which include the cell-cycle regulators Cdk and cyclins. For example, the human T-cell leukemia virus type I (HTLV-1) Tax transactivator protein acts as an early response gene by enhancing the activity of a cellular transcription factor. The oncogenic properties of the Tax protein include transformation of primary T-lymphocytes and fibroblasts through cooperation with the GTP-binding protein, Ras. Recently investigators have shown that Tax interacts with several PDZ-containing proteins. The PDZ domain, originally described in the *Drosophila* tumor suppressor protein Discs-Large, is common to membrane proteins thought to be involved in clustering receptors in growth factor signal transduction pathways (Rousset, R. et al. (1998) Oncogene 16:643-654).

Tumor-suppressor genes are involved in regulating cell proliferation. Mutations which cause reduced or loss of function in tumor-suppressor genes result in uncontrolled cell proliferation. For example, the retinoblastoma gene product (RB), in a non-phosphorylated state, binds several early-response genes and suppresses their transcription, thus blocking cell division. Phosphorylation of RB causes it to dissociate from the genes, releasing the suppression, and allowing cell division to proceed.

Other gene products involved in cell proliferation, differentiation, and apoptosis are yet to be discovered. One method currently being utilized to help identify such new molecules involves comparisons between quiescent and proliferative tissues. For example, a subtractive hybridization screen of human placental cytotrophoblast cells identified 20 genes whose expression levels rose due to

EGF induction of cell proliferation. (Morrish, D.W. et al. (1996) *Placenta* 17:431-441). Another method involves identification of molecules produced in cells treated with anti-tumorigenic agents, such as dithiolethiones. Presumably, the protective action of these anti-tumorigenic agents is associated with the induction of tumor suppressor gene products (Primiano, T. et al. (1996) *Carcinogenesis* 17:2297-2303).

In another example, the candidate tumor-suppressor gene ING1, that codes a nuclear protein, p33ING1, is involved in the negative regulation of cell proliferation. The action of p33ING1 is dependent upon the activity of another tumor-suppressor gene, p53. p53 is a cellular stress-responsive gene requiring the activity of p33ING1 to effectively induce growth inhibition of cells. p33ING1 and p53 have been shown to physically associate through immunoprecipitation studies (Garkavtsev, I. et al. (1998) *Nature* 391:295-298).

Apoptosis

Apoptosis is the genetically controlled process by which unneeded or defective cells undergo programmed cell death. Selective elimination of cells is as important for morphogenesis and tissue remodeling as is cell proliferation and differentiation. Lack of apoptosis may result in hyperplasia and other disorders associated with increased cell proliferation. Apoptosis is also a critical component of the immune response. Immune cells such as cytotoxic T-cells and natural killer cells prevent the spread of disease by inducing apoptosis in tumor cells and virus-infected cells. In addition, immune cells that fail to distinguish self molecules from foreign molecules must be eliminated by apoptosis to avoid an autoimmune response.

Apoptotic cells undergo distinct morphological changes. Hallmarks of apoptosis include cell shrinkage, nuclear and cytoplasmic condensation, and alterations in plasma membrane topology. Biochemically, apoptotic cells are characterized by increased intracellular calcium concentration, fragmentation of chromosomal DNA, and expression of novel cell surface components.

The molecular mechanisms of apoptosis are highly conserved, and many of the key protein regulators and effectors of apoptosis have been identified. Apoptosis generally proceeds in response to a signal which is transduced intracellularly and results in altered patterns of gene expression and protein activity. Signaling molecules such as hormones and cytokines are known both to stimulate and to inhibit apoptosis through interactions with cell surface receptors. Transcription factors also play an important role in the onset of apoptosis. A number of downstream effector molecules, particularly proteases such as the cysteine proteases called caspases, have been implicated in the degradation of cellular components and the proteolytic activation of other apoptotic effectors.

Aging and Senescence

Studies of the aging process or senescence have shown a number of characteristic cellular and

molecular changes (Fauci, A.S. et al. (1998) Harrison's Principles of Internal Medicine, McGraw-Hill, New York NY, p.37). These characteristics include increases in chromosome structural abnormalities, DNA cross-linking, incidence of single-stranded breaks in DNA, losses in DNA methylation, and degradation of telomere regions. In addition to these DNA changes, post-translational alterations of

5 proteins increase including deamidation, oxidation, cross-linking, and nonenzymatic glycosylation. Still further molecular changes occur in the mitochondria of aging cells through deterioration of structure. These changes eventually contribute to decreased function in every organ of the body.

The discovery of new cell cycle and proliferation proteins and the polynucleotides encoding them satisfies a need in the art by providing new compositions which are useful in the diagnosis,

10 prevention, and treatment of immune, developmental, and cell signaling disorders, and cell proliferative disorders including cancer.

SUMMARY OF THE INVENTION

The invention features purified polypeptides, cell cycle and proliferation proteins, referred to

15 collectively as "CCYPR" and individually as "CCYPR-1," "CCYPR-2," "CCYPR-3," "CCYPR-4," "CCYPR-5," "CCYPR-6," "CCYPR-7," "CCYPR-8," "CCYPR-9," "CCYPR-10," "CCYPR-11," "CCYPR-12," "CCYPR-13," "CCYPR-14," "CCYPR-15," "CCYPR-16," "CCYPR-17," "CCYPR-18," "CCYPR-19," "CCYPR-20," "CCYPR-21," "CCYPR-22," "CCYPR-23," "CCYPR-24," "CCYPR-25," "CCYPR-26," "CCYPR-27," "CCYPR-28," "CCYPR-29," "CCYPR-30," "CCYPR-

20 31," "CCYPR-32," "CCYPR-33," "CCYPR-34," "CCYPR-35," "CCYPR-36," "CCYPR-37," "CCYPR-38," "CCYPR-39," "CCYPR-40," "CCYPR-41," "CCYPR-42," "CCYPR-43," "CCYPR-44," "CCYPR-45," "CCYPR-46," "CCYPR-47," "CCYPR-48," "CCYPR-49," "CCYPR-50," "CCYPR-51," "CCYPR-52," "CCYPR-53," "CCYPR-54." In one aspect, the invention provides an isolated polypeptide comprising an amino acid sequence selected from the group consisting of a) an

25 amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54. In one alternative, the invention

30 provides an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:1-54.

The invention further provides an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-

54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54. In one alternative, the polynucleotide encodes a polypeptide selected from the group consisting of SEQ ID NO:1-54. In another alternative, the polynucleotide is selected from the group consisting of SEQ ID NO:55-108.

Additionally, the invention provides a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54. In one alternative, the invention provides a cell transformed with the recombinant polynucleotide. In another alternative, the invention provides a transgenic organism comprising the recombinant polynucleotide.

The invention also provides a method for producing a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54. The method comprises a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding the polypeptide, and b) recovering the polypeptide so expressed.

Additionally, the invention provides an isolated antibody which specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54.

The invention further provides an isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of a) a polynucleotide sequence selected from the group consisting of

SEQ ID NO:55-108, b) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:55-108, c) a polynucleotide sequence complementary to a), d) a polynucleotide sequence complementary to b), and e) an RNA equivalent of a)-d). In one alternative, the polynucleotide comprises at least 60 contiguous
5 nucleotides.

Additionally, the invention provides a method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide comprising a polynucleotide sequence selected from the group consisting of a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:55-108, b) a naturally occurring polynucleotide sequence having at least 70% sequence
10 identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:55-108, c) a polynucleotide sequence complementary to a), d) a polynucleotide sequence complementary to b), and e) an RNA equivalent of a)-d). The method comprises a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions
15 whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and b) detecting the presence or absence of said hybridization complex, and optionally, if present, the amount thereof. In one alternative, the probe comprises at least 60 contiguous nucleotides.

The invention further provides a method for detecting a target polynucleotide in a sample, said
20 target polynucleotide having a sequence of a polynucleotide comprising a polynucleotide sequence selected from the group consisting of a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:55-108, b) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:55-108, c) a polynucleotide sequence complementary to a), d) a polynucleotide sequence complementary to b), and e)
25 an RNA equivalent of a)-d). The method comprises a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

The invention further provides a pharmaceutical composition comprising an effective amount
30 of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid

sequence selected from the group consisting of SEQ ID NO:1-54, and a pharmaceutically acceptable excipient. In one embodiment, the pharmaceutical composition comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-54. The invention additionally provides a method of treating a disease or condition associated with decreased expression of functional CCYPR, comprising administering to a patient in need of such treatment the pharmaceutical composition.

The invention also provides a method for screening a compound for effectiveness as an agonist of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54. The method comprises a) exposing a sample comprising the polypeptide to a compound, and b) detecting agonist activity in the sample. In one alternative, the invention provides a pharmaceutical composition comprising an agonist compound identified by the method and a pharmaceutically acceptable excipient. In another alternative, the invention provides a method of treating a disease or condition associated with decreased expression of functional CCYPR, comprising administering to a patient in need of such treatment the pharmaceutical composition.

Additionally, the invention provides a method for screening a compound for effectiveness as an antagonist of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54. The method comprises a) exposing a sample comprising the polypeptide to a compound, and b) detecting antagonist activity in the sample. In one alternative, the invention provides a pharmaceutical composition comprising an antagonist compound identified by the method and a pharmaceutically acceptable excipient. In another alternative, the invention provides a method of treating a disease or condition associated with overexpression of functional CCYPR, comprising administering to a patient in need of such treatment the pharmaceutical composition.

The invention further provides a method of screening for a compound that specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group

consisting of SEQ ID NO:1-54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54. The method comprises a) combining the polypeptide with at least one test compound under suitable conditions, and b) detecting binding of the polypeptide to the test compound, thereby identifying a compound that specifically binds to the polypeptide.

The invention further provides a method of screening for a compound that modulates the activity of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-54. The method comprises a) combining the polypeptide with at least one test compound under conditions permissive for the activity of the polypeptide, b) assessing the activity of the polypeptide in the presence of the test compound, and c) comparing the activity of the polypeptide in the presence of the test compound with the activity of the polypeptide in the absence of the test compound, wherein a change in the activity of the polypeptide in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide.

The invention further provides a method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence selected from the group consisting of SEQ ID NO:55-108, the method comprising a) exposing a sample comprising the target polynucleotide to a compound, and b) detecting altered expression of the target polynucleotide.

The invention further provides a method for assessing toxicity of a test compound, said method comprising a) treating a biological sample containing nucleic acids with the test compound; b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide comprising a polynucleotide sequence selected from the group consisting of i) a polynucleotide sequence selected from the group consisting of SEQ ID NO:55-108, ii) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:55-108, iii) a polynucleotide sequence complementary to i), iv) a polynucleotide sequence complementary to ii), and v) an RNA equivalent of i)-iv). Hybridization occurs under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence selected from the group

consisting of SEQ ID NO:55-108, ii) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:55-108, iii) a polynucleotide sequence complementary to i), iv) a polynucleotide sequence complementary to ii), and v) an RNA equivalent of i)-iv). Alternatively, the target polynucleotide comprises a fragment of the above polynucleotide sequence; c) quantifying the amount of hybridization complex; and d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

BRIEF DESCRIPTION OF THE TABLES

Table 1 shows polypeptide and nucleotide sequence identification numbers (SEQ ID NOs), clone identification numbers (clone IDs), cDNA libraries, and cDNA fragments used to assemble full-length sequences encoding CCYPR.

Table 2 shows features of each polypeptide sequence, including potential motifs, homologous sequences, and methods, algorithms, and searchable databases used for analysis of CCYPR.

Table 3 shows selected fragments of each nucleic acid sequence; the tissue-specific expression patterns of each nucleic acid sequence as determined by northern analysis; diseases, disorders, or conditions associated with these tissues; and the vector into which each cDNA was cloned.

Table 4 describes the tissues used to construct the cDNA libraries from which cDNA clones encoding CCYPR were isolated.

Table 5 shows the tools, programs, and algorithms used to analyze the polynucleotides and polypeptides of the invention, along with applicable descriptions, references, and threshold parameters.

DESCRIPTION OF THE INVENTION

Before the present proteins, nucleotide sequences, and methods are described, it is understood that this invention is not limited to the particular machines, materials and methods described, as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise. Thus, for example, a reference to "a host cell" includes a plurality of such host cells, and a reference to "an antibody" is a reference to one or more antibodies and equivalents thereof known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any machines, materials, and methods similar or equivalent to those described herein can be used to practice or test the present invention, the preferred machines, materials and methods are now described.

- 5 All publications mentioned herein are cited for the purpose of describing and disclosing the cell lines, protocols, reagents and vectors which are reported in the publications and which might be used in connection with the invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

DEFINITIONS

- 10 "CCYPR" refers to the amino acid sequences of substantially purified CCYPR obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and human, and from any source, whether natural, synthetic, semi-synthetic, or recombinant.

- The term "agonist" refers to a molecule which intensifies or mimics the biological activity of CCYPR. Agonists may include proteins, nucleic acids, carbohydrates, small molecules, or any other
15 compound or composition which modulates the activity of CCYPR either by directly interacting with CCYPR or by acting on components of the biological pathway in which CCYPR participates.

- An "allelic variant" is an alternative form of the gene encoding CCYPR. Allelic variants may result from at least one mutation in the nucleic acid sequence and may result in altered mRNAs or in polypeptides whose structure or function may or may not be altered. A gene may have none, one, or
20 many allelic variants of its naturally occurring form. Common mutational changes which give rise to allelic variants are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

- "Altered" nucleic acid sequences encoding CCYPR include those sequences with deletions,
25 insertions, or substitutions of different nucleotides, resulting in a polypeptide the same as CCYPR or a polypeptide with at least one functional characteristic of CCYPR. Included within this definition are polymorphisms which may or may not be readily detectable using a particular oligonucleotide probe of the polynucleotide encoding CCYPR, and improper or unexpected hybridization to allelic variants, with a locus other than the normal chromosomal locus for the polynucleotide sequence encoding CCYPR.
30 The encoded protein may also be "altered," and may contain deletions, insertions, or substitutions of amino acid residues which produce a silent change and result in a functionally equivalent CCYPR. Deliberate amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the biological or immunological activity of CCYPR is retained. For example, negatively charged amino

acids may include aspartic acid and glutamic acid, and positively charged amino acids may include lysine and arginine. Amino acids with uncharged polar side chains having similar hydrophilicity values may include: asparagine and glutamine; and serine and threonine. Amino acids with uncharged side chains having similar hydrophilicity values may include: leucine, isoleucine, and
5 valine; glycine and alanine; and phenylalanine and tyrosine.

The terms "amino acid" and "amino acid sequence" refer to an oligopeptide, peptide, polypeptide, or protein sequence, or a fragment of any of these, and to naturally occurring or synthetic molecules. Where "amino acid sequence" is recited to refer to a sequence of a naturally occurring protein molecule, "amino acid sequence" and like terms are not meant to limit the amino acid sequence
10 to the complete native amino acid sequence associated with the recited protein molecule.

"Amplification" relates to the production of additional copies of a nucleic acid sequence. Amplification is generally carried out using polymerase chain reaction (PCR) technologies well known in the art.

The term "antagonist" refers to a molecule which inhibits or attenuates the biological activity of
15 CCYPR. Antagonists may include proteins such as antibodies, nucleic acids, carbohydrates, small molecules, or any other compound or composition which modulates the activity of CCYPR either by directly interacting with CCYPR or by acting on components of the biological pathway in which CCYPR participates.

The term "antibody" refers to intact immunoglobulin molecules as well as to fragments thereof,
20 such as Fab, F(ab')₂, and Fv fragments, which are capable of binding an epitopic determinant. Antibodies that bind CCYPR polypeptides can be prepared using intact polypeptides or using fragments containing small peptides of interest as the immunizing antigen. The polypeptide or oligopeptide used to immunize an animal (e.g., a mouse, a rat, or a rabbit) can be derived from the translation of RNA, or synthesized chemically, and can be conjugated to a carrier protein if desired. Commonly used carriers
25 that are chemically coupled to peptides include bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin (KLH). The coupled peptide is then used to immunize the animal.

The term "antigenic determinant" refers to that region of a molecule (i.e., an epitope) that makes contact with a particular antibody. When a protein or a fragment of a protein is used to immunize a host animal, numerous regions of the protein may induce the production of antibodies which
30 bind specifically to antigenic determinants (particular regions or three-dimensional structures on the protein). An antigenic determinant may compete with the intact antigen (i.e., the immunogen used to elicit the immune response) for binding to an antibody.

The term "antisense" refers to any composition capable of base-pairing with the "sense" (coding) strand of a specific nucleic acid sequence. Antisense compositions may include DNA; RNA;
35 peptide nucleic acid (PNA); oligonucleotides having modified backbone linkages such as

phosphorothioates, methylphosphonates, or benzylphosphonates; oligonucleotides having modified sugar groups such as 2'-methoxyethyl sugars or 2'-methoxyethoxy sugars; or oligonucleotides having modified bases such as 5-methyl cytosine, 2'-deoxyuracil, or 7-deaza-2'-deoxyguanosine. Antisense molecules may be produced by any method including chemical synthesis or transcription. Once

5 introduced into a cell, the complementary antisense molecule base-pairs with a naturally occurring nucleic acid sequence produced by the cell to form duplexes which block either transcription or translation. The designation "negative" or "minus" can refer to the antisense strand, and the designation "positive" or "plus" can refer to the sense strand of a reference DNA molecule.

The term "biologically active" refers to a protein having structural, regulatory, or biochemical

10 functions of a naturally occurring molecule. Likewise, "immunologically active" or "immunogenic" refers to the capability of the natural, recombinant, or synthetic CCYPR, or of any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

"Complementary" describes the relationship between two single-stranded nucleic acid

15 sequences that anneal by base-pairing. For example, 5'-AGT-3' pairs with its complement, 3'-TCA-5'.

A "composition comprising a given polynucleotide sequence" and a "composition comprising a given amino acid sequence" refer broadly to any composition containing the given polynucleotide or amino acid sequence. The composition may comprise a dry formulation or an aqueous solution.

20 Compositions comprising polynucleotide sequences encoding CCYPR or fragments of CCYPR may be employed as hybridization probes. The probes may be stored in freeze-dried form and may be associated with a stabilizing agent such as a carbohydrate. In hybridizations, the probe may be deployed in an aqueous solution containing salts (e.g., NaCl), detergents (e.g., sodium dodecyl sulfate; SDS), and other components (e.g., Denhardt's solution, dry milk, salmon sperm DNA, etc.).

25 "Consensus sequence" refers to a nucleic acid sequence which has been subjected to repeated DNA sequence analysis to resolve uncalled bases, extended using the XL-PCR kit (PE Biosystems, Foster City CA) in the 5' and/or the 3' direction, and resequenced, or which has been assembled from one or more overlapping cDNA, EST, or genomic DNA fragments using a computer program for fragment assembly, such as the GELVIEW fragment assembly system (GCG, Madison WI) or Phrap

30 (University of Washington, Seattle WA). Some sequences have been both extended and assembled to produce the consensus sequence.

"Conservative amino acid substitutions" are those substitutions that are predicted to least interfere with the properties of the original protein, i.e., the structure and especially the function of the protein is conserved and not significantly changed by such substitutions. The table below shows amino

acids which may be substituted for an original amino acid in a protein and which are regarded as conservative amino acid substitutions.

	Original Residue	Conservative Substitution
5	Ala	Gly, Ser
	Arg	His, Lys
	Asn	Asp, Gln, His
	Asp	Asn, Glu
	Cys	Ala, Ser
10	Gln	Asn, Glu, His
	Glu	Asp, Gln, His
	Gly	Ala
	His	Asn, Arg, Gln, Glu
	Ile	Leu, Val
15	Leu	Ile, Val
	Lys	Arg, Gln, Glu
	Met	Leu, Ile
	Phe	His, Met, Leu, Trp, Tyr
	Ser	Cys, Thr
20	Thr	Ser, Val
	Trp	Phe, Tyr
	Tyr	His, Phe, Trp
	Val	Ile, Leu, Thr

Conservative amino acid substitutions generally maintain (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a beta sheet or alpha helical conformation, (b) the charge or hydrophobicity of the molecule at the site of the substitution, and/or (c) the bulk of the side chain.

A "deletion" refers to a change in the amino acid or nucleotide sequence that results in the absence of one or more amino acid residues or nucleotides.

The term "derivative" refers to a chemically modified polynucleotide or polypeptide. Chemical modifications of a polynucleotide sequence can include, for example, replacement of hydrogen by an alkyl, acyl, hydroxyl, or amino group. A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is one modified by glycosylation, pegylation, or any similar process that retains at least one biological or immunological function of the polypeptide from which it was derived.

A "detectable label" refers to a reporter molecule or enzyme that is capable of generating a measurable signal and is covalently or noncovalently joined to a polynucleotide or polypeptide.

A "fragment" is a unique portion of CCYPR or the polynucleotide encoding CCYPR which is identical in sequence to but shorter in length than the parent sequence. A fragment may comprise up to the entire length of the defined sequence, minus one nucleotide/amino acid residue. For example, a fragment may comprise from 5 to 1000 contiguous nucleotides or amino acid residues. A fragment

used as a probe, primer, antigen, therapeutic molecule, or for other purposes, may be at least 5, 10, 15, 16, 20, 25, 30, 40, 50, 60, 75, 100, 150, 250 or at least 500 contiguous nucleotides or amino acid residues in length. Fragments may be preferentially selected from certain regions of a molecule. For example, a polypeptide fragment may comprise a certain length of contiguous amino acids selected from the first 250 or 500 amino acids (or first 25% or 50% of a polypeptide) as shown in a certain defined sequence. Clearly these lengths are exemplary, and any length that is supported by the specification, including the Sequence Listing, tables, and figures, may be encompassed by the present embodiments.

A fragment of SEQ ID NO:55-108 comprises a region of unique polynucleotide sequence that specifically identifies SEQ ID NO:55-108, for example, as distinct from any other sequence in the genome from which the fragment was obtained. A fragment of SEQ ID NO:55-108 is useful, for example, in hybridization and amplification technologies and in analogous methods that distinguish SEQ ID NO:55-108 from related polynucleotide sequences. The precise length of a fragment of SEQ ID NO:55-108 and the region of SEQ ID NO:55-108 to which the fragment corresponds are routinely determinable by one of ordinary skill in the art based on the intended purpose for the fragment.

A fragment of SEQ ID NO:1-54 is encoded by a fragment of SEQ ID NO:55-108. A fragment of SEQ ID NO:1-54 comprises a region of unique amino acid sequence that specifically identifies SEQ ID NO:1-54. For example, a fragment of SEQ ID NO:1-54 is useful as an immunogenic peptide for the development of antibodies that specifically recognize SEQ ID NO:1-54. The precise length of a fragment of SEQ ID NO:1-54 and the region of SEQ ID NO:1-54 to which the fragment corresponds are routinely determinable by one of ordinary skill in the art based on the intended purpose for the fragment.

A "full-length" polynucleotide sequence is one containing at least a translation initiation codon (e.g., methionine) followed by an open reading frame and a translation termination codon. A "full-length" polynucleotide sequence encodes a "full-length" polypeptide sequence.

"Homology" refers to sequence similarity or, interchangeably, sequence identity, between two or more polynucleotide sequences or two or more polypeptide sequences.

The terms "percent identity" and "% identity," as applied to polynucleotide sequences, refer to the percentage of residue matches between at least two polynucleotide sequences aligned using a standardized algorithm. Such an algorithm may insert, in a standardized and reproducible way, gaps in the sequences being compared in order to optimize alignment between two sequences, and therefore achieve a more meaningful comparison of the two sequences.

Percent identity between polynucleotide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence alignment program. This program is part of the LASERGENE software package, a suite of molecular

biological analysis programs (DNASTAR, Madison WI). CLUSTAL V is described in Higgins, D.G. and P.M. Sharp (1989) CABIOS 5:151-153 and in Higgins, D.G. et al. (1992) CABIOS 8:189-191. For pairwise alignments of polynucleotide sequences, the default parameters are set as follows: Ktuple=2, gap penalty=5, window=4, and "diagonals saved"=4. The "weighted" residue weight table is selected as the default. Percent identity is reported by CLUSTAL V as the "percent similarity" between aligned polynucleotide sequences.

Alternatively, a suite of commonly used and freely available sequence comparison algorithms is provided by the National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool (BLAST) (Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410), which is available from several sources, including the NCBI, Bethesda, MD, and on the Internet at <http://www.ncbi.nlm.nih.gov/BLAST/>. The BLAST software suite includes various sequence analysis programs including "blastn," that is used to align a known polynucleotide sequence with other polynucleotide sequences from a variety of databases. Also available is a tool called "BLAST 2 Sequences" that is used for direct pairwise comparison of two nucleotide sequences. "BLAST 2 Sequences" can be accessed and used interactively at <http://www.ncbi.nlm.nih.gov/gorf/bl2.html>. The "BLAST 2 Sequences" tool can be used for both blastn and blastp (discussed below). BLAST programs are commonly used with gap and other parameters set to default settings. For example, to compare two nucleotide sequences, one may use blastn with the "BLAST 2 Sequences" tool Version 2.0.12 (April-21-2000) set at default parameters. Such default parameters may be, for example:

Matrix: BLOSUM62
Reward for match: 1
Penalty for mismatch: -2
Open Gap: 5 and Extension Gap: 2 penalties
Gap x drop-off: 50
Expect: 10
Word Size: 11
Filter: on

Percent identity may be measured over the length of an entire defined sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined sequence, for instance, a fragment of at least 20, at least 30, at least 40, at least 50, at least 70, at least 100, or at least 200 contiguous nucleotides. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures, or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

Nucleic acid sequences that do not show a high degree of identity may nevertheless encode similar amino acid sequences due to the degeneracy of the genetic code. It is understood that changes in a nucleic acid sequence can be made using this degeneracy to produce multiple nucleic acid sequences that all encode substantially the same protein.

- 5 The phrases "percent identity" and "% identity," as applied to polypeptide sequences, refer to the percentage of residue matches between at least two polypeptide sequences aligned using a standardized algorithm. Methods of polypeptide sequence alignment are well-known. Some alignment methods take into account conservative amino acid substitutions. Such conservative substitutions, explained in more detail above, generally preserve the charge and hydrophobicity at the site of
- 10 substitution, thus preserving the structure (and therefore function) of the polypeptide.

- Percent identity between polypeptide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence alignment program (described and referenced above). For pairwise alignments of polypeptide sequences using CLUSTAL V, the default parameters are set as follows: Ktuple=1, gap penalty=3, window=5, and
- 15 "diagonals saved"=5. The PAM250 matrix is selected as the default residue weight table. As with polynucleotide alignments, the percent identity is reported by CLUSTAL V as the "percent similarity" between aligned polypeptide sequence pairs.

- Alternatively the NCBI BLAST software suite may be used. For example, for a pairwise comparison of two polypeptide sequences, one may use the "BLAST 2 Sequences" tool Version 2.0.12
- 20 (Apr-21-2000) with blastp set at default parameters. Such default parameters may be, for example:

Matrix: BLOSUM62

Open Gap: 11 and Extension Gap: 1 penalties

Gap x drop-off: 50

Expect: 10

- 25 *Word Size: 3*

Filter: on

- Percent identity may be measured over the length of an entire defined polypeptide sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined polypeptide sequence, for instance,
- 30 a fragment of at least 15, at least 20, at least 30, at least 40, at least 50, at least 70 or at least 150 contiguous residues. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

"Human artificial chromosomes" (HACs) are linear microchromosomes which may contain

DNA sequences of about 6 kb to 10 Mb in size, and which contain all of the elements required for chromosome replication, segregation and maintenance.

The term "humanized antibody" refers to an antibody molecule in which the amino acid sequence in the non-antigen binding regions has been altered so that the antibody more closely resembles a human antibody, and still retains its original binding ability.

"Hybridization" refers to the process by which a polynucleotide strand anneals with a complementary strand through base pairing under defined hybridization conditions. Specific hybridization is an indication that two nucleic acid sequences share a high degree of complementarity. Specific hybridization complexes form under permissive annealing conditions and remain hybridized after the "washing" step(s). The washing step(s) is particularly important in determining the stringency of the hybridization process, with more stringent conditions allowing less non-specific binding, i.e., binding between pairs of nucleic acid strands that are not perfectly matched. Permissive conditions for annealing of nucleic acid sequences are routinely determinable by one of ordinary skill in the art and may be consistent among hybridization experiments, whereas wash conditions may be varied among experiments to achieve the desired stringency, and therefore hybridization specificity. Permissive annealing conditions occur, for example, at 68°C in the presence of about 6 x SSC, about 1% (w/v) SDS, and about 100 µg/ml sheared, denatured salmon sperm DNA.

Generally, stringency of hybridization is expressed, in part, with reference to the temperature under which the wash step is carried out. Such wash temperatures are typically selected to be about 5°C to 20°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH. The T_m is the temperature (under defined ionic strength and pH) at which 50% of the target sequence hybridizes to a perfectly matched probe. An equation for calculating T_m and conditions for nucleic acid hybridization are well known and can be found in Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY; specifically see volume 2, chapter 9.

High stringency conditions for hybridization between polynucleotides of the present invention include wash conditions of 68°C in the presence of about 0.2 x SSC and about 0.1% SDS, for 1 hour. Alternatively, temperatures of about 65°C, 60°C, 55°C, or 42°C may be used. SSC concentration may be varied from about 0.1 to 2 x SSC, with SDS being present at about 0.1%. Typically, blocking reagents are used to block non-specific hybridization. Such blocking reagents include, for instance, sheared and denatured salmon sperm DNA at about 100-200 µg/ml. Organic solvent, such as formamide at a concentration of about 35-50% v/v, may also be used under particular circumstances, such as for RNA:DNA hybridizations. Useful variations on these wash conditions will be readily apparent to those of ordinary skill in the art. Hybridization, particularly under high stringency

conditions, may be suggestive of evolutionary similarity between the nucleotides. Such similarity is strongly indicative of a similar role for the nucleotides and their encoded polypeptides.

The term "hybridization complex" refers to a complex formed between two nucleic acid sequences by virtue of the formation of hydrogen bonds between complementary bases. A hybridization
5 complex may be formed in solution (e.g., C_0t or R_0t analysis) or formed between one nucleic acid sequence present in solution and another nucleic acid sequence immobilized on a solid support (e.g., paper, membranes, filters, chips, pins or glass slides, or any other appropriate substrate to which cells or their nucleic acids have been fixed).

The words "insertion" and "addition" refer to changes in an amino acid or nucleotide sequence
10 resulting in the addition of one or more amino acid residues or nucleotides, respectively.

"Immune response" can refer to conditions associated with inflammation, trauma, immune disorders, or infectious or genetic disease, etc. These conditions can be characterized by expression of various factors, e.g., cytokines, chemokines, and other signaling molecules, which may affect cellular and systemic defense systems.

An "immunogenic fragment" is a polypeptide or oligopeptide fragment of CCYPR which is
15 capable of eliciting an immune response when introduced into a living organism, for example, a mammal. The term "immunogenic fragment" also includes any polypeptide or oligopeptide fragment of CCYPR which is useful in any of the antibody production methods disclosed herein or known in the art.

The term "microarray" refers to an arrangement of a plurality of polynucleotides, polypeptides,
20 or other chemical compounds on a substrate.

The terms "element" and "array element" refer to a polynucleotide, polypeptide, or other chemical compound having a unique and defined position on a microarray.

The term "modulate" refers to a change in the activity of CCYPR. For example, modulation may cause an increase or a decrease in protein activity, binding characteristics, or any other biological,
25 functional, or immunological properties of CCYPR.

The phrases "nucleic acid" and "nucleic acid sequence" refer to a nucleotide, oligonucleotide, polynucleotide, or any fragment thereof. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA), or to any DNA-like or RNA-like material.

"Operably linked" refers to the situation in which a first nucleic acid sequence is placed in a
30 functional relationship with a second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Operably linked DNA sequences may be in close proximity or contiguous and, where necessary to join two protein coding regions, in the same reading frame.

35 "Peptide nucleic acid" (PNA) refers to an antisense molecule or anti-gene agent which

comprises an oligonucleotide of at least about 5 nucleotides in length linked to a peptide backbone of amino acid residues ending in lysine. The terminal lysine confers solubility to the composition. PNAs preferentially bind complementary single stranded DNA or RNA and stop transcript elongation, and may be pegylated to extend their lifespan in the cell.

- 5 "Post-translational modification" of an CCYPR may involve lipidation, glycosylation, phosphorylation, acetylation, racemization, proteolytic cleavage, and other modifications known in the art. These processes may occur synthetically or biochemically. Biochemical modifications will vary by cell type depending on the enzymatic milieu of CCYPR.

- "Probe" refers to nucleic acid sequences encoding CCYPR, their complements, or fragments thereof, which are used to detect identical, allelic or related nucleic acid sequences. Probes are isolated oligonucleotides or polynucleotides attached to a detectable label or reporter molecule. Typical labels include radioactive isotopes, ligands, chemiluminescent agents, and enzymes. "Primers" are short nucleic acids, usually DNA oligonucleotides, which may be annealed to a target polynucleotide by complementary base-pairing. The primer may then be extended along the target DNA strand by a DNA polymerase enzyme. Primer pairs can be used for amplification (and identification) of a nucleic acid sequence, e.g., by the polymerase chain reaction (PCR).
- 10
15

- Probes and primers as used in the present invention typically comprise at least 15 contiguous nucleotides of a known sequence. In order to enhance specificity, longer probes and primers may also be employed, such as probes and primers that comprise at least 20, 25, 30, 40, 50, 60, 70, 80, 90, 100, or at least 150 consecutive nucleotides of the disclosed nucleic acid sequences. Probes and primers may be considerably longer than these examples, and it is understood that any length supported by the specification, including the tables, figures, and Sequence Listing, may be used.
- 20

- Methods for preparing and using probes and primers are described in the references, for example Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY; Ausubel, F.M. et al., 1987, Current Protocols in Molecular Biology, Greene Publ. Assoc. & Wiley-Intersciences, New York NY; Innis, M. et al., 1990, PCR Protocols, A Guide to Methods and Applications, Academic Press, San Diego CA. PCR primer pairs can be derived from a known sequence, for example, by using computer programs intended for that purpose such as Primer (Version 0.5, 1991, Whitehead Institute for Biomedical Research, Cambridge MA).
- 25
30

Oligonucleotides for use as primers are selected using software known in the art for such purpose. For example, OLIGO 4.06 software is useful for the selection of PCR primer pairs of up to 100 nucleotides each, and for the analysis of oligonucleotides and larger polynucleotides of up to 5,000 nucleotides from an input polynucleotide sequence of up to 32 kilobases. Similar primer selection

- programs have incorporated additional features for expanded capabilities. For example, the PrimOU primer selection program (available to the public from the Genome Center at University of Texas South West Medical Center, Dallas TX) is capable of choosing specific primers from megabase sequences and is thus useful for designing primers on a genome-wide scope. The Primer3 primer selection
- 5 program (available to the public from the Whitehead Institute/MIT Center for Genome Research, Cambridge MA) allows the user to input a "mispriming library," in which sequences to avoid as primer binding sites are user-specified. Primer3 is useful, in particular, for the selection of oligonucleotides for microarrays. (The source code for the latter two primer selection programs may also be obtained from their respective sources and modified to meet the user's specific needs.) The PrimeGen program
- 10 (available to the public from the UK Human Genome Mapping Project Resource Centre, Cambridge UK) designs primers based on multiple sequence alignments, thereby allowing selection of primers that hybridize to either the most conserved or least conserved regions of aligned nucleic acid sequences. Hence, this program is useful for identification of both unique and conserved oligonucleotides and polynucleotide fragments. The oligonucleotides and polynucleotide fragments identified by any of the
- 15 above selection methods are useful in hybridization technologies, for example, as PCR or sequencing primers, microarray elements, or specific probes to identify fully or partially complementary polynucleotides in a sample of nucleic acids. Methods of oligonucleotide selection are not limited to those described above.

- A "recombinant nucleic acid" is a sequence that is not naturally occurring or has a sequence
- 20 that is made by an artificial combination of two or more otherwise separated segments of sequence. This artificial combination is often accomplished by chemical synthesis or, more commonly, by the artificial manipulation of isolated segments of nucleic acids, e.g., by genetic engineering techniques such as those described in Sambrook, supra. The term recombinant includes nucleic acids that have been altered solely by addition, substitution, or deletion of a portion of the nucleic acid. Frequently, a
- 25 recombinant nucleic acid may include a nucleic acid sequence operably linked to a promoter sequence. Such a recombinant nucleic acid may be part of a vector that is used, for example, to transform a cell.

- Alternatively, such recombinant nucleic acids may be part of a viral vector, e.g., based on a vaccinia virus, that could be used to vaccinate a mammal wherein the recombinant nucleic acid is expressed, inducing a protective immunological response in the mammal.

- 30 A "regulatory element" refers to a nucleic acid sequence usually derived from untranslated regions of a gene and includes enhancers, promoters, introns, and 5' and 3' untranslated regions (UTRs). Regulatory elements interact with host or viral proteins which control transcription, translation, or RNA stability.

"Reporter molecules" are chemical or biochemical moieties used for labeling a nucleic acid,

amino acid, or antibody. Reporter molecules include radionuclides; enzymes; fluorescent, chemiluminescent, or chromogenic agents; substrates; cofactors; inhibitors; magnetic particles; and other moieties known in the art.

5 An "RNA equivalent," in reference to a DNA sequence, is composed of the same linear sequence of nucleotides as the reference DNA sequence with the exception that all occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose.

10 The term "sample" is used in its broadest sense. A sample suspected of containing nucleic acids encoding CCYPR, or fragments thereof, or CCYPR itself, may comprise a bodily fluid; an extract from a cell, chromosome, organelle, or membrane isolated from a cell; a cell; genomic DNA, RNA, or cDNA, in solution or bound to a substrate; a tissue; a tissue print; etc.

15 The terms "specific binding" and "specifically binding" refer to that interaction between a protein or peptide and an agonist, an antibody, an antagonist, a small molecule, or any natural or synthetic binding composition. The interaction is dependent upon the presence of a particular structure of the protein, e.g., the antigenic determinant or epitope, recognized by the binding molecule. For example, if an antibody is specific for epitope "A," the presence of a polypeptide comprising the epitope A, or the presence of free unlabeled A, in a reaction containing free labeled A and the antibody will reduce the amount of labeled A that binds to the antibody.

20 The term "substantially purified" refers to nucleic acid or amino acid sequences that are removed from their natural environment and are isolated or separated, and are at least 60% free, preferably at least 75% free, and most preferably at least 90% free from other components with which they are naturally associated.

A "substitution" refers to the replacement of one or more amino acid residues or nucleotides by different amino acid residues or nucleotides, respectively.

25 "Substrate" refers to any suitable rigid or semi-rigid support including membranes, filters, chips, slides, wafers, fibers, magnetic or nonmagnetic beads, gels, tubing, plates, polymers, microparticles and capillaries. The substrate can have a variety of surface forms, such as wells, trenches, pins, channels and pores, to which polynucleotides or polypeptides are bound.

30 A "transcript image" refers to the collective pattern of gene expression by a particular cell type or tissue under given conditions at a given time.

"Transformation" describes a process by which exogenous DNA is introduced into a recipient cell. Transformation may occur under natural or artificial conditions according to various methods well known in the art, and may rely on any known method for the insertion of foreign nucleic acid sequences into a prokaryotic or eukaryotic host cell. The method for transformation is selected based on the type

of host cell being transformed and may include, but is not limited to, bacteriophage or viral infection, electroporation, heat shock, lipofection, and particle bombardment. The term "transformed" cells includes stably transformed cells in which the inserted DNA is capable of replication either as an autonomously replicating plasmid or as part of the host chromosome, as well as transiently transformed cells which express the inserted DNA or RNA for limited periods of time.

A "transgenic organism," as used herein, is any organism, including but not limited to animals and plants, in which one or more of the cells of the organism contains heterologous nucleic acid introduced by way of human intervention, such as by transgenic techniques well known in the art. The nucleic acid is introduced into the cell, directly or indirectly by introduction into a precursor of the cell, by way of deliberate genetic manipulation, such as by microinjection or by infection with a recombinant virus. The term genetic manipulation does not include classical cross-breeding, or in vitro fertilization, but rather is directed to the introduction of a recombinant DNA molecule. The transgenic organisms contemplated in accordance with the present invention include bacteria, cyanobacteria, fungi, plants, and animals. The isolated DNA of the present invention can be introduced into the host by methods known in the art, for example infection, transfection, transformation or transconjugation. Techniques for transferring the DNA of the present invention into such organisms are widely known and provided in references such as Sambrook et al. (1989), supra.

A "variant" of a particular nucleic acid sequence is defined as a nucleic acid sequence having at least 40% sequence identity to the particular nucleic acid sequence over a certain length of one of the nucleic acid sequences using blastn with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of nucleic acids may show, for example, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95% or at least 98% or greater sequence identity over a certain defined length. A variant may be described as, for example, an "allelic" (as defined above), "splice," "species," or "polymorphic" variant. A splice variant may have significant identity to a reference molecule, but will generally have a greater or lesser number of polynucleotides due to alternative splicing of exons during mRNA processing. The corresponding polypeptide may possess additional functional domains or lack domains that are present in the reference molecule. Species variants are polynucleotide sequences that vary from one species to another. The resulting polypeptides generally will have significant amino acid identity relative to each other. A polymorphic variant is a variation in the polynucleotide sequence of a particular gene between individuals of a given species. Polymorphic variants also may encompass "single nucleotide polymorphisms" (SNPs) in which the polynucleotide sequence varies by one nucleotide base. The presence of SNPs may be indicative of, for example, a certain population, a disease state, or a propensity for a disease state.

A "variant" of a particular polypeptide sequence is defined as a polypeptide sequence having at

least 40% sequence identity to the particular polypeptide sequence over a certain length of one of the polypeptide sequences using blastp with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of polypeptides may show, for example, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or at least 98% or greater sequence
 5 identity over a certain defined length of one of the polypeptides.

THE INVENTION

The invention is based on the discovery of new human cell cycle and proliferation proteins (CCYPR), the polynucleotides encoding CCYPR, and the use of these compositions for the diagnosis, treatment, or prevention of immune, developmental, and cell signaling disorders, and cell proliferative
 10 disorders including cancer.

Table 1 lists the Incyte clones used to assemble full length nucleotide sequences encoding CCYPR. Columns 1 and 2 show the sequence identification numbers (SEQ ID NOs) of the polypeptide and nucleotide sequences, respectively. Column 3 shows the clone IDs of the Incyte clones in which nucleic acids encoding each CCYPR were identified, and column 4 shows the cDNA libraries from
 15 which these clones were isolated. Column 5 shows Incyte clones and their corresponding cDNA libraries. Clones for which cDNA libraries are not indicated were derived from pooled cDNA libraries. In some cases, GenBank sequence identifiers are also shown in column 5. The Incyte clones and GenBank cDNA sequences, where indicated, in column 5 were used to assemble the consensus nucleotide sequence of each CCYPR and are useful as fragments in hybridization technologies.

The columns of Table 2 show various properties of each of the polypeptides of the invention: column 1 references the SEQ ID NO; column 2 shows the number of amino acid residues in each polypeptide; column 3 shows potential phosphorylation sites; column 4 shows potential glycosylation sites; column 5 shows the amino acid residues comprising signature sequences and motifs; column 6 shows homologous sequences as identified by BLAST analysis along with relevant citations, all of
 25 which are expressly incorporated by reference herein in their entirety; and column 7 shows analytical methods and in some cases, searchable databases to which the analytical methods were applied. The methods of column 7 were used to characterize each polypeptide through sequence homology and protein motifs.

The columns of Table 3 show the tissue-specificity and diseases, disorders, or conditions
 30 associated with nucleotide sequences encoding CCYPR. The first column of Table 3 lists the nucleotide SEQ ID NOs. Column 2 lists fragments of the nucleotide sequences of column 1. These fragments are useful, for example, in hybridization or amplification technologies to identify SEQ ID NO:55-108 and to distinguish between SEQ ID NO:55-108 and related polynucleotide sequences. The polypeptides encoded by these fragments are useful, for example, as immunogenic peptides. Column 3 lists tissue

categories which express CCYPR as a fraction of total tissues expressing CCYPR. Column 4 lists diseases, disorders, or conditions associated with those tissues expressing CCYPR as a fraction of total tissues expressing CCYPR. Column 5 lists the vectors used to subclone each cDNA library. Of particular note is the expression of SEQ ID NO:66 in inflammatory tissues. It should be noted that

5 SEQ ID NO:76 was found to be expressed predominantly in nervous tissue.

The columns of Table 4 show descriptions of the tissues used to construct the cDNA libraries from which cDNA clones encoding CCYPR were isolated. Column 1 references the nucleotide SEQ ID NOs, column 2 shows the cDNA libraries from which these clones were isolated, and column 3 shows the tissue origins and other descriptive information relevant to the cDNA libraries in column 2.

- 10 SEQ ID NO:61 maps to chromosome 5 within the interval from 141.40 to 142.60 centiMorgans. This interval also contains gene(s) and/or EST(s) associated with corneal dystrophy and deafness.

- SEQ ID NO:73 maps to chromosome 2 within the interval from 73.80 to 83.50 centiMorgans. This interval also contains gene(s) and/or EST(s) associated with hereditary nonpolyposis colorectal carcinoma and Muir-Torre syndrome. SEQ ID NO:74 maps to chromosome 19 within the interval
- 15 from 41.70 to 58.70 centiMorgans. SEQ ID NO:75 maps to chromosome 17 within the interval from 62.90 to 64.20 centiMorgans. This interval also contains gene(s) and/or EST(s) located within the human breast cancer (BRCA1) gene region. SEQ ID NO:76 maps to chromosome 1 within the interval from 143.30 to 153.90 centiMorgans, to chromosome 3 within the interval from 156.20 to
- 20 160.00 centiMorgans, and to chromosome X within the interval from 112.80 to 139.40 centiMorgans. The interval on chromosome X from 112.80 to 139.40 centiMorgans also contains gene(s) and/or EST(s) associated with X-linked agammaglobulinaemia.

- SEQ ID NO:77 maps to chromosome 23 within the interval from 173.60 to 179.80 centiMorgans, and to chromosome 11 within the interval from 136.90 centiMorgans to q-terminus.
- 25 SEQ ID NO:78 maps to chromosome 3 within the interval from 200.00 to 213.70 centiMorgans. SEQ ID NO:81 maps to chromosome 7 within the interval from 167.60 centiMorgans to q-terminus. SEQ ID NO:90 maps to chromosome 2 within the interval from 236.10 to 240.20 centiMorgans, to chromosome 3 within the interval from 16.50 to 43.00 centiMorgans, and to chromosome 6 within the interval from 124.20 to 126.50 centiMorgans. SEQ ID NO:91 maps to chromosome 2 within the
- 30 interval from 22.40 to 40.70 centiMorgans. SEQ ID NO:98 maps to chromosome 8 within the interval from 40.30 to 60.00 centiMorgans. SEQ ID NO:100 maps to chromosome 14 within the interval from 95.50 to 103.70 centiMorgans, and to chromosome 6 within the interval from 158.50 centiMorgans to q-terminus. SEQ ID NO:104 maps to chromosome 18 within the interval from 32.40 to 42.70 centiMorgans. SEQ ID NO:105 maps to chromosome 19 within the interval from 69.90 to
- 35 81.20 centiMorgans.

The invention also encompasses CCYPR variants. A preferred CCYPR variant is one which has at least about 80%, or alternatively at least about 90%, or even at least about 95% amino acid sequence identity to the CCYPR amino acid sequence, and which contains at least one functional or structural characteristic of CCYPR.

- 5 The invention also encompasses polynucleotides which encode CCYPR. In a particular embodiment, the invention encompasses a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:55-108, which encodes CCYPR. The polynucleotide sequences of SEQ ID NO:55-108, as presented in the Sequence Listing, embrace the equivalent RNA sequences, wherein occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone
- 10 is composed of ribose instead of deoxyribose.

- The invention also encompasses a variant of a polynucleotide sequence encoding CCYPR. In particular, such a variant polynucleotide sequence will have at least about 70%, or alternatively at least about 85%, or even at least about 95% polynucleotide sequence identity to the polynucleotide sequence encoding CCYPR. A particular aspect of the invention encompasses a variant of a polynucleotide
- 15 sequence comprising a sequence selected from the group consisting of SEQ ID NO:55-108 which has at least about 70%, or alternatively at least about 85%, or even at least about 95% polynucleotide sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:55-108. Any one of the polynucleotide variants described above can encode an amino acid sequence which contains at least one functional or structural characteristic of CCYPR.

- 20 It will be appreciated by those skilled in the art that as a result of the degeneracy of the genetic code, a multitude of polynucleotide sequences encoding CCYPR, some bearing minimal similarity to the polynucleotide sequences of any known and naturally occurring gene, may be produced. Thus, the invention contemplates each and every possible variation of polynucleotide sequence that could be made by selecting combinations based on possible codon choices. These combinations are made in
- 25 accordance with the standard triplet genetic code as applied to the polynucleotide sequence of naturally occurring CCYPR, and all such variations are to be considered as being specifically disclosed.

- Although nucleotide sequences which encode CCYPR and its variants are generally capable of hybridizing to the nucleotide sequence of the naturally occurring CCYPR under appropriately selected conditions of stringency, it may be advantageous to produce nucleotide sequences encoding CCYPR or
- 30 its derivatives possessing a substantially different codon usage, e.g., inclusion of non-naturally occurring codons. Codons may be selected to increase the rate at which expression of the peptide occurs in a particular prokaryotic or eukaryotic host in accordance with the frequency with which particular codons are utilized by the host. Other reasons for substantially altering the nucleotide sequence encoding CCYPR and its derivatives without altering the encoded amino acid sequences

include the production of RNA transcripts having more desirable properties, such as a greater half-life, than transcripts produced from the naturally occurring sequence.

The invention also encompasses production of DNA sequences which encode CCYPR and CCYPR derivatives, or fragments thereof, entirely by synthetic chemistry. After production, the synthetic sequence may be inserted into any of the many available expression vectors and cell systems using reagents well known in the art. Moreover, synthetic chemistry may be used to introduce mutations into a sequence encoding CCYPR or any fragment thereof.

Also encompassed by the invention are polynucleotide sequences that are capable of hybridizing to the claimed polynucleotide sequences, and, in particular, to those shown in SEQ ID NO:55-108 and fragments thereof under various conditions of stringency. (See, e.g., Wahl, G.M. and S.L. Berger (1987) *Methods Enzymol.* 152:399-407; Kimmel, A.R. (1987) *Methods Enzymol.* 152:507-511.) Hybridization conditions, including annealing and wash conditions, are described in "Definitions."

Methods for DNA sequencing are well known in the art and may be used to practice any of the embodiments of the invention. The methods may employ such enzymes as the Klenow fragment of DNA polymerase I, SEQUENASE (US Biochemical, Cleveland OH), Taq polymerase (PE Biosystems, Foster City CA), thermostable T7 polymerase (Amersham Pharmacia Biotech, Piscataway NJ), or combinations of polymerases and proofreading exonucleases such as those found in the ELONGASE amplification system (Life Technologies, Gaithersburg MD). Preferably, sequence preparation is automated with machines such as the MICROLAB 2200 liquid transfer system (Hamilton, Reno NV), PTC200 thermal cycler (MJ Research, Watertown MA) and ABI CATALYST 800 thermal cycler (PE Biosystems). Sequencing is then carried out using either the ABI 373 or 377 DNA sequencing system (PE Biosystems), the MEGABACE 1000 DNA sequencing system (Molecular Dynamics, Sunnyvale CA), or other systems known in the art. The resulting sequences are analyzed using a variety of algorithms which are well known in the art. (See, e.g., Ausubel, F.M. (1997) Short Protocols in Molecular Biology, John Wiley & Sons, New York NY, unit 7.7; Meyers, R.A. (1995) Molecular Biology and Biotechnology, Wiley VCH, New York NY, pp. 856-853.)

The nucleic acid sequences encoding CCYPR may be extended utilizing a partial nucleotide sequence and employing various PCR-based methods known in the art to detect upstream sequences, such as promoters and regulatory elements. For example, one method which may be employed, restriction-site PCR, uses universal and nested primers to amplify unknown sequence from genomic DNA within a cloning vector. (See, e.g., Sarkar, G. (1993) *PCR Methods Applic.* 2:318-322.) Another method, inverse PCR, uses primers that extend in divergent directions to amplify unknown sequence from a circularized template. The template is derived from restriction fragments comprising a

- known genomic locus and surrounding sequences. (See, e.g., Triglia, T. et al. (1988) *Nucleic Acids Res.* 16:8186.) A third method, capture PCR, involves PCR amplification of DNA fragments adjacent to known sequences in human and yeast artificial chromosome DNA. (See, e.g., Lagerstrom, M. et al. (1991) *PCR Methods Applic.* 1:111-119.) In this method, multiple restriction enzyme digestions and
- 5 ligations may be used to insert an engineered double-stranded sequence into a region of unknown sequence before performing PCR. Other methods which may be used to retrieve unknown sequences are known in the art. (See, e.g., Parker, J.D. et al. (1991) *Nucleic Acids Res.* 19:3055-3060). Additionally, one may use PCR, nested primers, and PROMOTERFINDER libraries (Clontech, Palo Alto CA) to walk genomic DNA. This procedure avoids the need to screen libraries and is useful in
- 10 finding intron/exon junctions. For all PCR-based methods, primers may be designed using commercially available software, such as OLIGO 4.06 Primer Analysis software (National Biosciences, Plymouth MN) or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the template at temperatures of about 68°C to 72°C.
- 15 When screening for full-length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. In addition, random-primed libraries, which often include sequences containing the 5' regions of genes, are preferable for situations in which an oligo d(T) library does not yield a full-length cDNA. Genomic libraries may be useful for extension of sequence into 5' non-transcribed regulatory regions.
- 20 Capillary electrophoresis systems which are commercially available may be used to analyze the size or confirm the nucleotide sequence of sequencing or PCR products. In particular, capillary sequencing may employ flowable polymers for electrophoretic separation, four different nucleotide-specific, laser-stimulated fluorescent dyes, and a charge coupled device camera for detection of the emitted wavelengths. Output/light intensity may be converted to electrical signal using appropriate
- 25 software (e.g., GENOTYPER and SEQUENCE NAVIGATOR, PE Biosystems), and the entire process from loading of samples to computer analysis and electronic data display may be computer controlled. Capillary electrophoresis is especially preferable for sequencing small DNA fragments which may be present in limited amounts in a particular sample.
- In another embodiment of the invention, polynucleotide sequences or fragments thereof which
- 30 encode CCYPR may be cloned in recombinant DNA molecules that direct expression of CCYPR, or fragments or functional equivalents thereof, in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be produced and used to express CCYPR.

The nucleotide sequences of the present invention can be engineered using methods generally

known in the art in order to alter CCYPR-encoding sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. For example, oligonucleotide-mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth.

The nucleotides of the present invention may be subjected to DNA shuffling techniques such as MOLECULARBREEDING (Maxygen Inc., Santa Clara CA; described in U.S. Patent Number 5,837,458; Chang, C.-C. et al. (1999) Nat. Biotechnol. 17:793-797; Christians, F.C. et al. (1999) Nat. Biotechnol. 17:259-264; and Cramer, A. et al. (1996) Nat. Biotechnol. 14:315-319) to alter or improve the biological properties of CCYPR, such as its biological or enzymatic activity or its ability to bind to other molecules or compounds. DNA shuffling is a process by which a library of gene variants is produced using PCR-mediated recombination of gene fragments. The library is then subjected to selection or screening procedures that identify those gene variants with the desired properties. These preferred variants may then be pooled and further subjected to recursive rounds of DNA shuffling and selection/screening. Thus, genetic diversity is created through "artificial" breeding and rapid molecular evolution. For example, fragments of a single gene containing random point mutations may be recombined, screened, and then reshuffled until the desired properties are optimized. Alternatively, fragments of a given gene may be recombined with fragments of homologous genes in the same gene family, either from the same or different species, thereby maximizing the genetic diversity of multiple naturally occurring genes in a directed and controllable manner.

In another embodiment, sequences encoding CCYPR may be synthesized, in whole or in part, using chemical methods well known in the art. (See, e.g., Caruthers, M.H. et al. (1980) Nucleic Acids Symp. Ser. 7:215-223; and Horn, T. et al. (1980) Nucleic Acids Symp. Ser. 7:225-232.) Alternatively, CCYPR itself or a fragment thereof may be synthesized using chemical methods. For example, peptide synthesis can be performed using various solution-phase or solid-phase techniques. (See, e.g., Creighton, T. (1984) Proteins, Structures and Molecular Properties, WH Freeman, New York NY, pp. 55-60; and Roberge, J.Y. et al. (1995) Science 269:202-204.) Automated synthesis may be achieved using the ABI 431A peptide synthesizer (PE Biosystems). Additionally, the amino acid sequence of CCYPR, or any part thereof, may be altered during direct synthesis and/or combined with sequences from other proteins, or any part thereof, to produce a variant polypeptide or a polypeptide having a sequence of a naturally occurring polypeptide.

The peptide may be substantially purified by preparative high performance liquid chromatography. (See, e.g., Chiez, R.M. and F.Z. Regnier (1990) Methods Enzymol. 182:392-421.)

The composition of the synthetic peptides may be confirmed by amino acid analysis or by sequencing. (See, e.g., Creighton, supra, pp. 28-53.)

In order to express a biologically active CCYPR, the nucleotide sequences encoding CCYPR or derivatives thereof may be inserted into an appropriate expression vector, i.e., a vector which contains the necessary elements for transcriptional and translational control of the inserted coding sequence in a suitable host. These elements include regulatory sequences, such as enhancers, constitutive and inducible promoters, and 5' and 3' untranslated regions in the vector and in polynucleotide sequences encoding CCYPR. Such elements may vary in their strength and specificity. Specific initiation signals may also be used to achieve more efficient translation of sequences encoding CCYPR. Such signals include the ATG initiation codon and adjacent sequences, e.g. the Kozak sequence. In cases where sequences encoding CCYPR and its initiation codon and upstream regulatory sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a fragment thereof, is inserted, exogenous translational control signals including an in-frame ATG initiation codon should be provided by the vector. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate for the particular host cell system used. (See, e.g., Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162.)

Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding CCYPR and appropriate transcriptional and translational control elements. These methods include in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. (See, e.g., Sambrook, J. et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview NY, ch. 4, 8, and 16-17; Ausubel, F.M. et al. (1995) Current Protocols in Molecular Biology, John Wiley & Sons, New York NY, ch. 9, 13, and 16.)

A variety of expression vector/host systems may be utilized to contain and express sequences encoding CCYPR. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with viral expression vectors (e.g., baculovirus); plant cell systems transformed with viral expression vectors (e.g., cauliflower mosaic virus, CaMV, or tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems. (See, e.g., Sambrook, supra; Ausubel, supra; Van Heeke, G. and S.M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509; Bitter, G.A. et al. (1987) *Methods Enzymol.* 153:516-544; Scorer, C.A. et al. (1994) *Bio/Technology* 12:181-184; Engelhard, E.K. et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:3224-3227; Sandig, V. et al. (1996) *Hum. Gene Ther.* 7:1937-1945; Takamatsu,

- N. (1987) *EMBO J.* 6:307-311; Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; Winter, J. et al. (1991) *Results Probl. Cell Differ.* 17:85-105; The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196; Logan, J. and T. Shenk (1984) *Proc. Natl. Acad. Sci. USA* 81:3655-3659; and Harrington, J.J. et al. (1997) *Nat. Genet.* 15:345-355.) Expression vectors derived from retroviruses, adenoviruses, or herpes or vaccinia viruses, or from various bacterial plasmids, may be used for delivery of nucleotide sequences to the targeted organ, tissue, or cell population. (See, e.g., Di Nicola, M. et al. (1998) *Cancer Gen. Ther.* 5(6):350-356; Yu, M. et al., (1993) *Proc. Natl. Acad. Sci. USA* 90(13):6340-6344; Buller, R.M. et al. (1985) *Nature* 317(6040):813-815; McGregor, D.P. et al. (1994) *Mol. Immunol.* 31(3):219-226; and Verma, I.M. and N. Somia (1997) *Nature* 389:239-242.)
- The invention is not limited by the host cell employed.

- In bacterial systems, a number of cloning and expression vectors may be selected depending upon the use intended for polynucleotide sequences encoding CCYPR. For example, routine cloning, subcloning, and propagation of polynucleotide sequences encoding CCYPR can be achieved using a multifunctional *E. coli* vector such as PBLUESCRIPT (Stratagene, La Jolla CA) or PSPT01 plasmid (Life Technologies). Ligation of sequences encoding CCYPR into the vector's multiple cloning site disrupts the *lacZ* gene, allowing a colorimetric screening procedure for identification of transformed bacteria containing recombinant molecules. In addition, these vectors may be useful for *in vitro* transcription, dideoxy sequencing, single strand rescue with helper phage, and creation of nested deletions in the cloned sequence. (See, e.g., Van Heeke, G. and S.M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509.) When large quantities of CCYPR are needed, e.g. for the production of antibodies, vectors which direct high level expression of CCYPR may be used. For example, vectors containing the strong, inducible T5 or T7 bacteriophage promoter may be used.

- Yeast expression systems may be used for production of CCYPR. A number of vectors containing constitutive or inducible promoters, such as alpha factor, alcohol oxidase, and PGH promoters, may be used in the yeast *Saccharomyces cerevisiae* or *Pichia pastoris*. In addition, such vectors direct either the secretion or intracellular retention of expressed proteins and enable integration of foreign sequences into the host genome for stable propagation. (See, e.g., Ausubel, 1995, *supra*; Bitter, *supra*; and Scorer, *supra*.)

- Plant systems may also be used for expression of CCYPR. Transcription of sequences encoding CCYPR may be driven viral promoters, e.g., the 35S and 19S promoters of CaMV used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311). Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used. (See, e.g., Coruzzi, *supra*; Broglie, *supra*; and Winter, *supra*.) These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated

transfection. (See, e.g., The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196.)

In mammalian cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, sequences encoding CCYPR may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain infective virus which expresses CCYPR in host cells. (See, e.g., Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. USA 81:3655-3659.) In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells. SV40 or EBV-based vectors may also be used for high-level protein expression.

Human artificial chromosomes (HACs) may also be employed to deliver larger fragments of DNA than can be contained in and expressed from a plasmid. HACs of about 6 kb to 10 Mb are constructed and delivered via conventional delivery methods (liposomes, polycationic amino polymers, or vesicles) for therapeutic purposes. (See, e.g., Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355.)

For long term production of recombinant proteins in mammalian systems, stable expression of CCYPR in cell lines is preferred. For example, sequences encoding CCYPR can be transformed into cell lines using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for about 1 to 2 days in enriched media before being switched to selective media. The purpose of the selectable marker is to confer resistance to a selective agent, and its presence allows growth and recovery of cells which successfully express the introduced sequences. Resistant clones of stably transformed cells may be propagated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase and adenine phosphoribosyltransferase genes, for use in *tk* and *apv* cells, respectively. (See, e.g., Wigler, M. et al. (1977) Cell 11:223-232; Lowy, I. et al. (1980) Cell 22:817-823.) Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example, *dhfr* confers resistance to methotrexate; *neo* confers resistance to the aminoglycosides neomycin and G-418; and *als* and *pat* confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively. (See, e.g., Wigler, M. et al. (1980) Proc. Natl. Acad. Sci. USA 77:3567-3570; Colbere-Garapin, F. et al. (1981) J. Mol. Biol. 150:1-14.) Additional selectable genes have been described, e.g., *trpB* and *hisD*, which alter cellular requirements for metabolites. (See, e.g., Hartman, S.C. and R.C. Mulligan (1988) Proc. Natl. Acad. Sci. USA 85:8047-8051.) Visible markers, e.g., anthocyanins, green fluorescent proteins (GFP; Clontech), B

glucuronidase and its substrate β -glucuronide, or luciferase and its substrate luciferin may be used. These markers can be used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system. (See, e.g., Rhodes, C.A. (1995) *Methods Mol. Biol.* 55:121-131.)

- 5 Although the presence/absence of marker gene expression suggests that the gene of interest is also present, the presence and expression of the gene may need to be confirmed. For example, if the sequence encoding CCYPR is inserted within a marker gene sequence, transformed cells containing sequences encoding CCYPR can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a sequence encoding CCYPR under the control of a single
10 promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

- In general, host cells that contain the nucleic acid sequence encoding CCYPR and that express CCYPR may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations, PCR
15 amplification, and protein bioassay or immunoassay techniques which include membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein sequences.

- Immunological methods for detecting and measuring the expression of CCYPR using either specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), and fluorescence
20 activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on CCYPR is preferred, but a competitive binding assay may be employed. These and other assays are well known in the art. (See, e.g., Hampton, R. et al. (1990) Serological Methods, a Laboratory Manual, APS Press, St. Paul MN, Sect. IV; Coligan, J.E. et al. (1997) Current Protocols in Immunology, Greene Pub. Associates and Wiley-Interscience, New
25 York NY; and Pound, J.D. (1998) Immunochemical Protocols, Humana Press, Totowa NJ.)

- A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides encoding CCYPR include oligolabeling, nick translation, end-labeling, or PCR amplification using a labeled nucleotide.
30 Alternatively, the sequences encoding CCYPR, or any fragments thereof, may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes *in vitro* by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits, such as those provided by Amersham Pharmacia Biotech, Promega

(Madison WI), and US Biochemical. Suitable reporter molecules or labels which may be used for ease of detection include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with nucleotide sequences encoding CCYPR may be cultured under
5 conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a transformed cell may be secreted or retained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode CCYPR may be designed to contain signal sequences which direct secretion of CCYPR through a prokaryotic or eukaryotic cell membrane.

10 In addition, a host cell strain may be chosen for its ability to modulate expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" or "pro" form of the protein may also be used to specify protein targeting, folding, and/or activity. Different host cells
15 which have specific cellular machinery and characteristic mechanisms for post-translational activities (e.g., CHO, HeLa, MDCK, HEK293, and WI38) are available from the American Type Culture Collection (ATCC, Manassas VA) and may be chosen to ensure the correct modification and processing of the foreign protein.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid
20 sequences encoding CCYPR may be ligated to a heterologous sequence resulting in translation of a fusion protein in any of the aforementioned host systems. For example, a chimeric CCYPR protein containing a heterologous moiety that can be recognized by a commercially available antibody may facilitate the screening of peptide libraries for inhibitors of CCYPR activity. Heterologous protein and peptide moieties may also facilitate purification of fusion proteins using commercially available affinity
25 matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose binding protein (MBP), thioredoxin (Trx), calmodulin binding peptide (CBP), 6-His, FLAG, *c-myc*, and hemagglutinin (HA). GST, MBP, Trx, CBP, and 6-His enable purification of their cognate fusion proteins on immobilized glutathione, maltose, phenylarsine oxide, calmodulin, and metal-chelate resins, respectively. FLAG, *c-myc*, and hemagglutinin (HA) enable immunoaffinity purification of fusion
30 proteins using commercially available monoclonal and polyclonal antibodies that specifically recognize these epitope tags. A fusion protein may also be engineered to contain a proteolytic cleavage site located between the CCYPR encoding sequence and the heterologous protein sequence, so that CCYPR may be cleaved away from the heterologous moiety following purification. Methods for fusion protein expression and purification are discussed in Ausubel (1995, supra, ch. 10). A variety of commercially

available kits may also be used to facilitate expression and purification of fusion proteins.

In a further embodiment of the invention, synthesis of radiolabeled CCYPR may be achieved in vitro using the TNT rabbit reticulocyte lysate or wheat germ extract system (Promega). These systems couple transcription and translation of protein-coding sequences operably associated with the T7, T3, or SP6 promoters. Translation takes place in the presence of a radiolabeled amino acid precursor, for example, ³⁵S-methionine.

CCYPR of the present invention or fragments thereof may be used to screen for compounds that specifically bind to CCYPR. At least one and up to a plurality of test compounds may be screened for specific binding to CCYPR. Examples of test compounds include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

In one embodiment, the compound thus identified is closely related to the natural ligand of CCYPR, e.g., a ligand or fragment thereof, a natural substrate, a structural or functional mimetic, or a natural binding partner. (See, Coligan, J.E. et al. (1991) Current Protocols in Immunology 1(2): Chapter 5.) Similarly, the compound can be closely related to the natural receptor to which CCYPR binds, or to at least a fragment of the receptor, e.g., the ligand binding site. In either case, the compound can be rationally designed using known techniques. In one embodiment, screening for these compounds involves producing appropriate cells which express CCYPR, either as a secreted protein or on the cell membrane. Preferred cells include cells from mammals, yeast, Drosophila, or E. coli. Cells expressing CCYPR or cell membrane fractions which contain CCYPR are then contacted with a test compound and binding, stimulation, or inhibition of activity of either CCYPR or the compound is analyzed.

An assay may simply test binding of a test compound to the polypeptide, wherein binding is detected by a fluorophore, radioisotope, enzyme conjugate, or other detectable label. For example, the assay may comprise the steps of combining at least one test compound with CCYPR, either in solution or affixed to a solid support, and detecting the binding of CCYPR to the compound. Alternatively, the assay may detect or measure binding of a test compound in the presence of a labeled competitor. Additionally, the assay may be carried out using cell-free preparations, chemical libraries, or natural product mixtures, and the test compound(s) may be free in solution or affixed to a solid support.

CCYPR of the present invention or fragments thereof may be used to screen for compounds that modulate the activity of CCYPR. Such compounds may include agonists, antagonists, or partial or inverse agonists. In one embodiment, an assay is performed under conditions permissive for CCYPR activity, wherein CCYPR is combined with at least one test compound, and the activity of CCYPR in the presence of a test compound is compared with the activity of CCYPR in the absence of the test compound. A change in the activity of CCYPR in the presence of the test compound is

indicative of a compound that modulates the activity of CCYPR. Alternatively, a test compound is combined with an in vitro or cell-free system comprising CCYPR under conditions suitable for CCYPR activity, and the assay is performed. In either of these assays, a test compound which modulates the activity of CCYPR may do so indirectly and need not come in direct contact with the test compound. At least one and up to a plurality of test compounds may be screened.

In another embodiment, polynucleotides encoding CCYPR or their mammalian homologs may be "knocked out" in an animal model system using homologous recombination in embryonic stem (ES) cells. Such techniques are well known in the art and are useful for the generation of animal models of human disease. (See, e.g., U.S. Patent No. 5,175,383 and U.S. Patent No. 5,767,337.) For example, mouse ES cells, such as the mouse 129/SvJ cell line, are derived from the early mouse embryo and grown in culture. The ES cells are transformed with a vector containing the gene of interest disrupted by a marker gene, e.g., the neomycin phosphotransferase gene (neo; Capecchi, M.R. (1989) Science 244:1288-1292). The vector integrates into the corresponding region of the host genome by homologous recombination. Alternatively, homologous recombination takes place using the Cre-loxP system to knockout a gene of interest in a tissue- or developmental stage-specific manner (Marth, J.D. (1996) Clin. Invest. 97:1999-2002; Wagner, K.U. et al. (1997) Nucleic Acids Res. 25:4323-4330). Transformed ES cells are identified and microinjected into mouse cell blastocysts such as those from the C57BL/6 mouse strain. The blastocysts are surgically transferred to pseudopregnant dams, and the resulting chimeric progeny are genotyped and bred to produce heterozygous or homozygous strains. Transgenic animals thus generated may be tested with potential therapeutic or toxic agents.

Polynucleotides encoding CCYPR may also be manipulated in vitro in ES cells derived from human blastocysts. Human ES cells have the potential to differentiate into at least eight separate cell lineages including endoderm, mesoderm, and ectodermal cell types. These cell lineages differentiate into, for example, neural cells, hematopoietic lineages, and cardiomyocytes (Thomson, J.A. et al. (1998) Science 282:1145-1147).

Polynucleotides encoding CCYPR can also be used to create "knockin" humanized animals (pigs) or transgenic animals (mice or rats) to model human disease. With knockin technology, a region of a polynucleotide encoding CCYPR is injected into animal ES cells, and the injected sequence integrates into the animal cell genome. Transformed cells are injected into blastulae, and the blastulae are implanted as described above. Transgenic progeny or inbred lines are studied and treated with potential pharmaceutical agents to obtain information on treatment of a human disease. Alternatively, a mammal inbred to overexpress CCYPR, e.g., by secreting CCYPR in its milk, may also serve as a convenient source of that protein (Janne, J. et al. (1998) Biotechnol. Annu. Rev. 4:55-74).

THERAPEUTICS

Chemical and structural similarity, e.g., in the context of sequences and motifs, exists between regions of CCYPR and cell cycle and proliferation proteins. In addition, the expression of CCYPR is closely associated with inflammation, trauma, cell proliferation and cancer. Therefore,

- 5 CCYPR appears to play a role in immune, developmental, and cell signaling disorders, and cell proliferative disorders including cancer. In the treatment of disorders associated with increased CCYPR expression or activity, it is desirable to decrease the expression or activity of CCYPR. In the treatment of disorders associated with decreased CCYPR expression or activity, it is desirable to increase the expression or activity of CCYPR.
- 10 Therefore, in one embodiment, CCYPR or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of CCYPR. Examples of such disorders include, but are not limited to, an immune disorder such as inflammation, actinic keratosis, acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia,
- 15 arteriosclerosis, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), bronchitis, bursitis, cholecystitis, cirrhosis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves'
- 20 disease, Hashimoto's thyroiditis, paroxysmal nocturnal hemoglobinuria, hepatitis, hypereosinophilia, irritable bowel syndrome, mixed connective tissue disorder (MCTD), multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, myelofibrosis, osteoarthritis, osteoporosis, pancreatitis, polycythemia vera, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic
- 25 sclerosis, primary thrombocythemia, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, trauma, and hematopoietic cancer including lymphoma, leukemia, and myeloma; a developmental disorder such as renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, Duchenne and Becker muscular dystrophy, epilepsy,
- 30 gonadal dysgenesis, WAGR syndrome (Wilms' tumor, aniridia, genitourinary abnormalities, and mental retardation), Smith-Magenis syndrome, myelodysplastic syndrome, hereditary mucoepithelial dysplasia, hereditary keratodermas, hereditary neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Sydenham's chorea and cerebral palsy, spina bifida, anencephaly, craniorachischisis, congenital glaucoma, cataract,
- 35 sensorineural hearing loss, and disorders of immune cell activation; a cell signaling disorder including

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endocrine disorders such as disorders of the hypothalamus and pituitary resulting from lesions such as primary brain tumors, adenomas, infarction associated with pregnancy, hypophysectomy, aneurysms, vascular malformations, thrombosis, infections, immunological disorders, and complications due to head trauma; disorders associated with hyperpituitarism including acromegaly, gigantism, and

5 syndrome of inappropriate antidiuretic hormone (ADH) secretion (SIADH) often caused by benign adenoma; disorders associated with hypothyroidism including goiter, myxedema, acute thyroiditis associated with bacterial infection; disorders associated with hyperparathyroidism including Conn disease (chronic hypercalcemia); pancreatic disorders such as Type I or Type II diabetes mellitus and associated complications; disorders associated with the adrenals such as hyperplasia, carcinoma, or

10 adenoma of the adrenal cortex, hypertension associated with alkalosis; disorders associated with gonadal steroid hormones such as: in women, abnormal prolactin production, infertility, including tubal disease, ovulatory defects, and endometriosis, perturbations of the menstrual cycle, polycystic ovarian disease, ovarian hyperstimulation syndrome, an endometrial or ovarian tumor, a uterine fibroid, autoimmune disorders, an ectopic pregnancy, teratogenesis, hyperprolactinemia, isolated

15 gonadotropin deficiency, amenorrhea, galactorrhea, hermaphroditism, hirsutism and virilization, breast cancer, and fibrocystic breast disease; and, in post-menopausal women, osteoporosis; and, in men, Leydig cell deficiency, male climacteric phase, germinal cell aplasia, hypergonadal disorders associated with Leydig cell tumors, androgen resistance associated with absence of androgen receptors, syndrome of 5 α -reductase, a disruption of spermatogenesis, abnormal sperm physiology,

20 cancer of the testis, cancer of the prostate, benign prostatic hyperplasia, prostatitis, Peyronie's disease, impotence, carcinoma of the male breast, and gynecomastia; and a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma,

25 myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus.

In another embodiment, a vector capable of expressing CCYPR or a fragment or derivative

30 thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of CCYPR including, but not limited to, those described above.

In a further embodiment, a pharmaceutical composition comprising a substantially purified CCYPR in conjunction with a suitable pharmaceutical carrier may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of CCYPR including, but not

35 limited to, those provided above.

In still another embodiment, an agonist which modulates the activity of CCYPR may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of CCYPR including, but not limited to, those listed above.

In a further embodiment, an antagonist of CCYPR may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of CCYPR. Examples of such disorders include, but are not limited to, those immune, developmental, and cell signaling disorders, and cell proliferative disorders including cancer, described above. In one aspect, an antibody which specifically binds CCYPR may be used directly as an antagonist or indirectly as a targeting or delivery mechanism for bringing a pharmaceutical agent to cells or tissues which express CCYPR.

In an additional embodiment, a vector expressing the complement of the polynucleotide encoding CCYPR may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of CCYPR including, but not limited to, those described above.

In other embodiments, any of the proteins, antagonists, antibodies, agonists, complementary sequences, or vectors of the invention may be administered in combination with other appropriate therapeutic agents. Selection of the appropriate agents for use in combination therapy may be made by one of ordinary skill in the art, according to conventional pharmaceutical principles. The combination of therapeutic agents may act synergistically to effect the treatment or prevention of the various disorders described above. Using this approach, one may be able to achieve therapeutic efficacy with lower dosages of each agent, thus reducing the potential for adverse side effects.

An antagonist of CCYPR may be produced using methods which are generally known in the art. In particular, purified CCYPR may be used to produce antibodies or to screen libraries of pharmaceutical agents to identify those which specifically bind CCYPR. Antibodies to CCYPR may also be generated using methods that are well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, and single chain antibodies, Fab fragments, and fragments produced by a Fab expression library. Neutralizing antibodies (i.e., those which inhibit dimer formation) are generally preferred for therapeutic use.

For the production of antibodies, various hosts including goats, rabbits, rats, mice, humans, and others may be immunized by injection with CCYPR or with any fragment or oligopeptide thereof which has immunogenic properties. Depending on the host species, various adjuvants may be used to increase immunological response. Such adjuvants include, but are not limited to, Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, KLH, and dinitrophenol. Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are especially preferable.

It is preferred that the oligopeptides, peptides, or fragments used to induce antibodies to

CCYPR have an amino acid sequence consisting of at least about 5 amino acids, and generally will consist of at least about 10 amino acids. It is also preferable that these oligopeptides, peptides, or fragments are identical to a portion of the amino acid sequence of the natural protein. Short stretches of CCYPR amino acids may be fused with those of another protein, such as KLH, and antibodies to the
 5 chimeric molecule may be produced.

Monoclonal antibodies to CCYPR may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-hybridoma technique. (See, e.g., Kohler, G. et al. (1975) *Nature* 256:495-497; Kozbor, D. et al. (1985) *J. Immunol. Methods* 81:31-42; Cote, R.J. et al. (1983) *Proc. Natl. Acad. Sci. USA* 80:2026-2030; and
 10 Cole, S.P. et al. (1984) *Mol. Cell Biol.* 62:109-120.)

In addition, techniques developed for the production of "chimeric antibodies," such as the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity, can be used. (See, e.g., Morrison, S.L. et al. (1984) *Proc. Natl. Acad. Sci. USA* 81:6851-6855; Neuberger, M.S. et al. (1984) *Nature* 312:604-608; and Takeda,
 15 S. et al. (1985) *Nature* 314:452-454.) Alternatively, techniques described for the production of single chain antibodies may be adapted, using methods known in the art, to produce CCYPR-specific single chain antibodies. Antibodies with related specificity, but of distinct idiotypic composition, may be generated by chain shuffling from random combinatorial immunoglobulin libraries. (See, e.g., Burton,
 20 D.R. (1991) *Proc. Natl. Acad. Sci. USA* 88:10134-10137.)

Antibodies may also be produced by inducing *in vivo* production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature. (See, e.g., Orlandi, R. et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:3833-3837; Winter,
 G. et al. (1991) *Nature* 349:293-299.)

Antibody fragments which contain specific binding sites for CCYPR may also be generated. For example, such fragments include, but are not limited to, F(ab')₂ fragments produced by pepsin digestion of the antibody molecule and Fab fragments generated by reducing the disulfide bridges of the F(ab')₂ fragments. Alternatively, Fab expression libraries may be constructed to allow rapid and easy
 25 identification of monoclonal Fab fragments with the desired specificity. (See, e.g., Huse, W.D. et al. (1989) *Science* 246:1275-1281.)
 30

Various immunoassays may be used for screening to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between CCYPR and its

specific antibody. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering CCYPR epitopes is generally used, but a competitive binding assay may also be employed (Pound, supra).

Various methods such as Scatchard analysis in conjunction with radioimmunoassay techniques may be used to assess the affinity of antibodies for CCYPR. Affinity is expressed as an association constant, K_a , which is defined as the molar concentration of CCYPR-antibody complex divided by the molar concentrations of free antigen and free antibody under equilibrium conditions. The K_a determined for a preparation of polyclonal antibodies, which are heterogeneous in their affinities for multiple CCYPR epitopes, represents the average affinity, or avidity, of the antibodies for CCYPR. The K_a determined for a preparation of monoclonal antibodies, which are monospecific for a particular CCYPR epitope, represents a true measure of affinity. High-affinity antibody preparations with K_a ranging from about 10^9 to 10^{12} L/mole are preferred for use in immunoassays in which the CCYPR-antibody complex must withstand rigorous manipulations. Low-affinity antibody preparations with K_a ranging from about 10^6 to 10^7 L/mole are preferred for use in immunopurification and similar procedures which ultimately require dissociation of CCYPR, preferably in active form, from the antibody (Catty, D. (1988) Antibodies, Volume I: A Practical Approach, IRL Press, Washington DC; Liddell, J.E. and A. Cryer (1991) A Practical Guide to Monoclonal Antibodies, John Wiley & Sons, New York NY).

The titer and avidity of polyclonal antibody preparations may be further evaluated to determine the quality and suitability of such preparations for certain downstream applications. For example, a polyclonal antibody preparation containing at least 1-2 mg specific antibody/ml, preferably 5-10 mg specific antibody/ml, is generally employed in procedures requiring precipitation of CCYPR-antibody complexes. Procedures for evaluating antibody specificity, titer, and avidity, and guidelines for antibody quality and usage in various applications, are generally available. (See, e.g., Catty, supra, and Coligan et al., supra.)

In another embodiment of the invention, the polynucleotides encoding CCYPR, or any fragment or complement thereof, may be used for therapeutic purposes. In one aspect, modifications of gene expression can be achieved by designing complementary sequences or antisense molecules (DNA, RNA, PNA, or modified oligonucleotides) to the coding or regulatory regions of the gene encoding CCYPR. Such technology is well known in the art, and antisense oligonucleotides or larger fragments can be designed from various locations along the coding or control regions of sequences encoding CCYPR. (See, e.g., Agrawal, S., ed. (1996) Antisense Therapeutics, Humana Press Inc., Totawa NJ.)

In therapeutic use, any gene delivery system suitable for introduction of the antisense sequences into appropriate target cells can be used. Antisense sequences can be delivered intracellularly in the form of an expression plasmid which, upon transcription, produces a sequence

- complementary to at least a portion of the cellular sequence encoding the target protein. (See, e.g., Slater, J.E. et al. (1998) *J. Allergy Clin. Immunol.* 102(3):469-475; and Scanlon, K.J. et al. (1995) 9(13):1288-1296.) Antisense sequences can also be introduced intracellularly through the use of viral vectors, such as retrovirus and adeno-associated virus vectors. (See, e.g., Miller, A.D. (1990) *Blood* 76:271; Ausubel, *supra*; Uckert, W. and W. Walther (1994) *Pharmacol. Ther.* 63(3):323-347.) Other gene delivery mechanisms include liposome-derived systems, artificial viral envelopes, and other systems known in the art. (See, e.g., Rossi, J.J. (1995) *Br. Med. Bull.* 51(1):217-225; Boado, R.J. et al. (1998) *J. Pharm. Sci.* 87(11):1308-1315; and Morris, M.C. et al. (1997) *Nucleic Acids Res.* 25(14):2730-2736.)
- 10 In another embodiment of the invention, polynucleotides encoding CCYPR may be used for somatic or germline gene therapy. Gene therapy may be performed to (i) correct a genetic deficiency (e.g., in the cases of severe combined immunodeficiency (SCID)-X1 disease characterized by X-linked inheritance (Cavazzana-Calvo, M. et al. (2000) *Science* 288:669-672), severe combined immunodeficiency syndrome associated with an inherited adenosine deaminase (ADA) deficiency
- 15 (Blaese, R.M. et al. (1995) *Science* 270:475-480; Bordignon, C. et al. (1995) *Science* 270:470-475), cystic fibrosis (Zabner, J. et al. (1993) *Cell* 75:207-216; Crystal, R.G. et al. (1995) *Hum. Gene Therapy* 6:643-666; Crystal, R.G. et al. (1995) *Hum. Gene Therapy* 6:667-703), thalassemias, familial hypercholesterolemia, and hemophilia resulting from Factor VIII or Factor IX deficiencies (Crystal, R.G. (1995) *Science* 270:404-410; Verma, I.M. and Somia, N. (1997) *Nature* 389:239-242)), (ii)
- 20 express a conditionally lethal gene product (e.g., in the case of cancers which result from unregulated cell proliferation), or (iii) express a protein which affords protection against intracellular parasites (e.g., against human retroviruses, such as human immunodeficiency virus (HIV) (Baltimore, D. (1988) *Nature* 335:395-396; Poeschla, E. et al. (1996) *Proc. Natl. Acad. Sci. USA.* 93:11395-11399), hepatitis B or C virus (HBV, HCV); fungal parasites, such as Candida albicans and Paracoccidioides
- 25 brasiliensis; and protozoan parasites such as Plasmodium falciparum and Trypanosoma cruzi). In the case where a genetic deficiency in CCYPR expression or regulation causes disease, the expression of CCYPR from an appropriate population of transduced cells may alleviate the clinical manifestations caused by the genetic deficiency.

- In a further embodiment of the invention, diseases or disorders caused by deficiencies in
- 30 CCYPR are treated by constructing mammalian expression vectors encoding CCYPR and introducing these vectors by mechanical means into CCYPR-deficient cells. Mechanical transfer technologies for use with cells *in vivo* or *ex vitro* include (i) direct DNA microinjection into individual cells, (ii) ballistic gold particle delivery, (iii) liposome-mediated transfection, (iv) receptor-mediated gene transfer, and (v) the use of DNA transposons (Morgan, R.A. and W.F. Anderson (1993) *Annu. Rev. Biochem.* 62:191-
- 35 217; Ivics, Z. (1997) *Cell* 91:501-510; Boulay, J.-L. and H. Récipon (1998) *Curr. Opin. Biotechnol.*

9:445-450).

- Expression vectors that may be effective for the expression of CCYPR include, but are not limited to, the PCDNA 3.1, EPITAG, PRCCMV2, PREP, PVAX vectors (Invitrogen, Carlsbad CA), PCMV-SCRIPT, PCMV-TAG, PEGSH/PERV (Stratagene, La Jolla CA), and PTET-OFF,
- 5 PTET-ON, PTRE2, PTRE2-LUC, PTK-HYG (Clontech, Palo Alto CA). CCYPR may be expressed using (i) a constitutively active promoter, (e.g., from cytomegalovirus (CMV), Rous sarcoma virus (RSV), SV40 virus, thymidine kinase (TK), or β -actin genes), (ii) an inducible promoter (e.g., the tetracycline-regulated promoter (Gossen, M. and H. Bujard (1992) Proc. Natl. Acad. Sci. USA 89:5547-5551; Gossen, M. et al. (1995) Science 268:1766-1769; Rossi, F.M.V. and H.M. Blau (1998)
 - 10 Curr. Opin. Biotechnol. 9:451-456), commercially available in the T-REX plasmid (Invitrogen)); the ecodyson-inducible promoter (available in the plasmids PVGRXR and PIND; Invitrogen); the FK506/rapamycin inducible promoter; or the RU486/mifepristone inducible promoter (Rossi, F.M.V. and H.M. Blau, *supra*)), or (iii) a tissue-specific promoter or the native promoter of the endogenous gene encoding CCYPR from a normal individual.
 - 15 Commercially available liposome transformation kits (e.g., the PERFECT LIPID TRANSFECTION KIT, available from Invitrogen) allow one with ordinary skill in the art to deliver polynucleotides to target cells in culture and require minimal effort to optimize experimental parameters. In the alternative, transformation is performed using the calcium phosphate method (Graham, F.L. and A.J. Eb (1973) Virology 52:456-467), or by electroporation (Neumann, E. et al.
 - 20 (1982) EMBO J. 1:841-845). The introduction of DNA to primary cells requires modification of these standardized mammalian transfection protocols.

- In another embodiment of the invention, diseases or disorders caused by genetic defects with respect to CCYPR expression are treated by constructing a retrovirus vector consisting of (i) the polynucleotide encoding CCYPR under the control of an independent promoter or the retrovirus long
- 25 terminal repeat (LTR) promoter, (ii) appropriate RNA packaging signals, and (iii) a Rev-responsive element (RRE) along with additional retrovirus *cis*-acting RNA sequences and coding sequences required for efficient vector propagation. Retrovirus vectors (e.g., PFB and PFBNEO) are commercially available (Stratagene) and are based on published data (Riviere, I. et al. (1995) Proc. Natl. Acad. Sci. USA 92:6733-6737), incorporated by reference herein. The vector is propagated in an
 - 30 appropriate vector producing cell line (VPCL) that expresses an envelope gene with a tropism for receptors on the target cells or a promiscuous envelope protein such as VSVg (Armentano, D. et al. (1987) J. Virol. 61:1647-1650; Bender, M.A. et al. (1987) J. Virol. 61:1639-1646; Adam, M.A. and A.D. Miller (1988) J. Virol. 62:3802-3806; Dull, T. et al. (1998) J. Virol. 72:8463-8471; Zufferey, R. et al. (1998) J. Virol. 72:9873-9880). U.S. Patent Number 5,910,434 to Rigg ("Method for obtaining

retrovirus packaging cell lines producing high transducing efficiency retroviral supernatant") discloses a method for obtaining retrovirus packaging cell lines and is hereby incorporated by reference.

Propagation of retrovirus vectors, transduction of a population of cells (e.g., CD4⁺ T-cells), and the return of transduced cells to a patient are procedures well known to persons skilled in the art of gene therapy and have been well documented (Ranga, U. et al. (1997) J. Virol. 71:7020-7029; Bauer, G. et al. (1997) Blood 89:2259-2267; Bonyhadi, M.L. (1997) J. Virol. 71:4707-4716; Ranga, U. et al. (1998) Proc. Natl. Acad. Sci. USA 95:1201-1206; Su, L. (1997) Blood 89:2283-2290).

In the alternative, an adenovirus-based gene therapy delivery system is used to deliver polynucleotides encoding CCYPR to cells which have one or more genetic abnormalities with respect to the expression of CCYPR. The construction and packaging of adenovirus-based vectors are well known to those with ordinary skill in the art. Replication defective adenovirus vectors have proven to be versatile for importing genes encoding immunoregulatory proteins into intact islets in the pancreas (Csete, M.E. et al. (1995) Transplantation 27:263-268). Potentially useful adenoviral vectors are described in U.S. Patent Number 5,707,618 to Armentano ("Adenovirus vectors for gene therapy"), hereby incorporated by reference. For adenoviral vectors, see also Antinozzi, P.A. et al. (1999) Annu. Rev. Nutr. 19:511-544; and Verma, I.M. and N. Somia (1997) Nature 18:389:239-242, both incorporated by reference herein.

In another alternative, a herpes-based, gene therapy delivery system is used to deliver polynucleotides encoding CCYPR to target cells which have one or more genetic abnormalities with respect to the expression of CCYPR. The use of herpes simplex virus (HSV)-based vectors may be especially valuable for introducing CCYPR to cells of the central nervous system, for which HSV has a tropism. The construction and packaging of herpes-based vectors are well known to those with ordinary skill in the art. A replication-competent herpes simplex virus (HSV) type 1-based vector has been used to deliver a reporter gene to the eyes of primates (Liu, X. et al. (1999) Exp. Eye Res. 169:385-395). The construction of a HSV-1 virus vector has also been disclosed in detail in U.S. Patent Number 5,804,413 to DeLuca ("Herpes simplex virus strains for gene transfer"), which is hereby incorporated by reference. U.S. Patent Number 5,804,413 teaches the use of recombinant HSV d92 which consists of a genome containing at least one exogenous gene to be transferred to a cell under the control of the appropriate promoter for purposes including human gene therapy. Also taught by this patent are the construction and use of recombinant HSV strains deleted for ICP4, ICP27 and ICP22. For HSV vectors, see also Goins, W.F. et al. (1999) J. Virol. 73:519-532 and Xu, H. et al. (1994) Dev. Biol. 163:152-161, hereby incorporated by reference. The manipulation of cloned herpesvirus sequences, the generation of recombinant virus following the transfection of multiple plasmids containing different segments of the large herpesvirus genomes, the growth and propagation of

herpesvirus, and the infection of cells with herpesvirus are techniques well known to those of ordinary skill in the art.

In another alternative, an alphavirus (positive, single-stranded RNA virus) vector is used to deliver polynucleotides encoding CCYPR to target cells. The biology of the prototypic alphavirus, Semliki Forest Virus (SFV), has been studied extensively and gene transfer vectors have been based on the SFV genome (Garoff, H. and K.-J. Li (1998) *Curr. Opin. Biotech.* 9:464-469). During alphavirus RNA replication, a subgenomic RNA is generated that normally encodes the viral capsid proteins. This subgenomic RNA replicates to higher levels than the full-length genomic RNA, resulting in the overproduction of capsid proteins relative to the viral proteins with enzymatic activity (e.g., protease and polymerase). Similarly, inserting the coding sequence for CCYPR into the alphavirus genome in place of the capsid-coding region results in the production of a large number of CCYPR-coding RNAs and the synthesis of high levels of CCYPR in vector transduced cells. While alphavirus infection is typically associated with cell lysis within a few days, the ability to establish a persistent infection in hamster normal kidney cells (BHK-21) with a variant of Sindbis virus (SIN) indicates that the lytic replication of alphaviruses can be altered to suit the needs of the gene therapy application (Dryga, S.A. et al. (1997) *Virology* 228:74-83). The wide host range of alphaviruses will allow the introduction of CCYPR into a variety of cell types. The specific transduction of a subset of cells in a population may require the sorting of cells prior to transduction. The methods of manipulating infectious cDNA clones of alphaviruses, performing alphavirus cDNA and RNA transfections, and performing alphavirus infections, are well known to those with ordinary skill in the art.

Oligonucleotides derived from the transcription initiation site, e.g., between about positions -10 and +10 from the start site, may also be employed to inhibit gene expression. Similarly, inhibition can be achieved using triple helix base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or regulatory molecules. Recent therapeutic advances using triplex DNA have been described in the literature. (See, e.g., Gee, J.E. et al. (1994) in Huber, B.E. and B.I. Carr, Molecular and Immunologic Approaches, Futura Publishing, Mt. Kisco NY, pp. 163-177.) A complementary sequence or antisense molecule may also be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

Ribozymes, enzymatic RNA molecules, may also be used to catalyze the specific cleavage of RNA. The mechanism of ribozyme action involves sequence-specific hybridization of the ribozyme molecule to complementary target RNA, followed by endonucleolytic cleavage. For example, engineered hammerhead motif ribozyme molecules may specifically and efficiently catalyze endonucleolytic cleavage of sequences encoding CCYPR.

Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites, including the following sequences: GUA, GUU, and GUC. Once identified, short RNA sequences of between 15 and 20 ribonucleotides, corresponding to the region of the target gene containing the cleavage site, may be evaluated for secondary structural features which may render the oligonucleotide inoperable. The suitability of candidate targets may also be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays.

Complementary ribonucleic acid molecules and ribozymes of the invention may be prepared by any method known in the art for the synthesis of nucleic acid molecules. These include techniques for chemically synthesizing oligonucleotides such as solid phase phosphoramidite chemical synthesis. Alternatively, RNA molecules may be generated by in vitro and in vivo transcription of DNA sequences encoding CCYPR. Such DNA sequences may be incorporated into a wide variety of vectors with suitable RNA polymerase promoters such as T7 or SP6. Alternatively, these cDNA constructs that synthesize complementary RNA, constitutively or inducibly, can be introduced into cell lines, cells, or tissues.

RNA molecules may be modified to increase intracellular stability and half-life. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends of the molecule, or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the backbone of the molecule. This concept is inherent in the production of PNAs and can be extended in all of these molecules by the inclusion of nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, cytidine, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

An additional embodiment of the invention encompasses a method for screening for a compound which is effective in altering expression of a polynucleotide encoding CCYPR.

Compounds which may be effective in altering expression of a specific polynucleotide may include, but are not limited to, oligonucleotides, antisense oligonucleotides, triple helix-forming oligonucleotides, transcription factors and other polypeptide transcriptional regulators, and non-macromolecular chemical entities which are capable of interacting with specific polynucleotide sequences. Effective compounds may alter polynucleotide expression by acting as either inhibitors or promoters of polynucleotide expression. Thus, in the treatment of disorders associated with increased CCYPR expression or activity, a compound which specifically inhibits expression of the polynucleotide encoding CCYPR may be therapeutically useful, and in the treatment of disorders associated with decreased CCYPR expression or activity, a compound which specifically promotes expression of the polynucleotide encoding CCYPR may be therapeutically useful.

At least one, and up to a plurality, of test compounds may be screened for effectiveness in

altering expression of a specific polynucleotide. A test compound may be obtained by any method commonly known in the art, including chemical modification of a compound known to be effective in altering polynucleotide expression; selection from an existing, commercially-available or proprietary library of naturally-occurring or non-natural chemical compounds; rational design of a compound
5 based on chemical and/or structural properties of the target polynucleotide; and selection from a library of chemical compounds created combinatorially or randomly. A sample comprising a polynucleotide encoding CCYPR is exposed to at least one test compound thus obtained. The sample may comprise, for example, an intact or permeabilized cell, or an in vitro cell-free or reconstituted biochemical system. Alterations in the expression of a polynucleotide encoding CCYPR are assayed
10 by any method commonly known in the art. Typically, the expression of a specific nucleotide is detected by hybridization with a probe having a nucleotide sequence complementary to the sequence of the polynucleotide encoding CCYPR. The amount of hybridization may be quantified, thus forming the basis for a comparison of the expression of the polynucleotide both with and without exposure to one or more test compounds. Detection of a change in the expression of a polynucleotide
15 exposed to a test compound indicates that the test compound is effective in altering the expression of the polynucleotide. A screen for a compound effective in altering expression of a specific polynucleotide can be carried out, for example, using a Schizosaccharomyces pombe gene expression system (Atkins, D. et al. (1999) U.S. Patent No. 5,932,435; Arndt, G.M. et al. (2000) Nucleic Acids Res. 28:E15) or a human cell line such as HeLa cell (Clarke, M.L. et al. (2000) Biochem. Biophys. Res. Commun. 268:8-13). A particular embodiment of the present invention involves screening a
20 combinatorial library of oligonucleotides (such as deoxyribonucleotides, ribonucleotides, peptide nucleic acids, and modified oligonucleotides) for antisense activity against a specific polynucleotide sequence (Bruce, T.W. et al. (1997) U.S. Patent No. 5,686,242; Bruce, T.W. et al. (2000) U.S. Patent No. 6,022,691).

25 Many methods for introducing vectors into cells or tissues are available and equally suitable for use in vivo, in vitro, and ex vivo. For ex vivo therapy, vectors may be introduced into stem cells taken from the patient and clonally propagated for autologous transplant back into that same patient. Delivery by transfection, by liposome injections, or by polycationic amino polymers may be achieved using methods which are well known in the art. (See, e.g., Goldman, C.K. et al. (1997) Nat.
30 Biotechnol. 15:462-466.)

Any of the therapeutic methods described above may be applied to any subject in need of such therapy, including, for example, mammals such as humans, dogs, cats, cows, horses, rabbits, and monkeys.

An additional embodiment of the invention relates to the administration of a pharmaceutical
35 composition which generally comprises an active ingredient formulated with a pharmaceutically

acceptable excipient. Excipients may include, for example, sugars, starches, celluloses, gums, and proteins. Various formulations are commonly known and are thoroughly discussed in the latest edition of Remington's Pharmaceutical Sciences (Maack Publishing, Easton PA). Such pharmaceutical compositions may consist of CCYPR, antibodies to CCYPR, and mimetics, agonists, antagonists, or
5 inhibitors of CCYPR.

The pharmaceutical compositions utilized in this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, pulmonary, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means.

10 Pharmaceutical compositions for pulmonary administration may be prepared in liquid or dry powder form. These compositions are generally aerosolized immediately prior to inhalation by the patient. In the case of small molecules (e.g. traditional low molecular weight organic drugs), aerosol delivery of fast-acting formulations is well-known in the art. In the case of macromolecules (e.g. larger peptides and proteins), recent developments in the field of pulmonary delivery via the alveolar region of
15 the lung have enabled the practical delivery of drugs such as insulin to blood circulation (see, e.g., Patton, J.S. et al., U.S. Patent No. 5,997,848). Pulmonary delivery has the advantage of administration without needle injection, and obviates the need for potentially toxic penetration enhancers.

Pharmaceutical compositions suitable for use in the invention include compositions wherein the active ingredients are contained in an effective amount to achieve the intended purpose. The
20 determination of an effective dose is well within the capability of those skilled in the art.

Specialized forms of pharmaceutical compositions may be prepared for direct intracellular delivery of macromolecules comprising CCYPR or fragments thereof. For example, liposome preparations containing a cell-impermeable macromolecule may promote cell fusion and intracellular delivery of the macromolecule. Alternatively, CCYPR or a fragment thereof may be joined to a short
25 cationic N-terminal portion from the HIV Tat-1 protein. Fusion proteins thus generated have been found to transduce into the cells of all tissues, including the brain, in a mouse model system (Schwarze, S.R. et al. (1999) Science 285:1569-1572).

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays, e.g., of neoplastic cells, or in animal models such as mice, rats, rabbits, dogs, monkeys,
30 or pigs. An animal model may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans.

A therapeutically effective dose refers to that amount of active ingredient, for example CCYPR or fragments thereof, antibodies of CCYPR, and agonists, antagonists or inhibitors of CCYPR, which

ameliorates the symptoms or condition. Therapeutic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or with experimental animals, such as by calculating the ED₅₀ (the dose therapeutically effective in 50% of the population) or LD₅₀ (the dose lethal to 50% of the population) statistics. The dose ratio of toxic to therapeutic effects is the therapeutic index, which can be expressed as the LD₅₀/ED₅₀ ratio. Pharmaceutical compositions which exhibit large therapeutic indices are preferred. The data obtained from cell culture assays and animal studies are used to formulate a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that includes the ED₅₀ with little or no toxicity. The dosage varies within this range depending upon the dosage form employed, the sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors related to the subject requiring treatment. Dosage and administration are adjusted to provide sufficient levels of the active moiety or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, the general health of the subject, the age, weight, and gender of the subject, time and frequency of administration, drug combination(s), reaction sensitivities, and response to therapy. Long-acting pharmaceutical compositions may be administered every 3 to 4 days, every week, or biweekly depending on the half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from about 0.1 μ g to 100,000 μ g, up to a total dose of about 1 gram, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

DIAGNOSTICS

In another embodiment, antibodies which specifically bind CCYPR may be used for the diagnosis of disorders characterized by expression of CCYPR, or in assays to monitor patients being treated with CCYPR or agonists, antagonists, or inhibitors of CCYPR. Antibodies useful for diagnostic purposes may be prepared in the same manner as described above for therapeutics. Diagnostic assays for CCYPR include methods which utilize the antibody and a label to detect CCYPR in human body fluids or in extracts of cells or tissues. The antibodies may be used with or without modification, and may be labeled by covalent or non-covalent attachment of a reporter molecule. A wide variety of reporter molecules, several of which are described above, are known in the art and may be used.

A variety of protocols for measuring CCYPR, including ELISAs, RIAs, and FACS, are known

in the art and provide a basis for diagnosing altered or abnormal levels of CCYPR expression. Normal or standard values for CCYPR expression are established by combining body fluids or cell extracts taken from normal mammalian subjects, for example, human subjects, with antibody to CCYPR under conditions suitable for complex formation. The amount of standard complex formation may be

5 quantitated by various methods, such as photometric means. Quantities of CCYPR expressed in subject, control, and disease samples from biopsied tissues are compared with the standard values. Deviation between standard and subject values establishes the parameters for diagnosing disease.

In another embodiment of the invention, the polynucleotides encoding CCYPR may be used for diagnostic purposes. The polynucleotides which may be used include oligonucleotide sequences,

10 complementary RNA and DNA molecules, and PNAs. The polynucleotides may be used to detect and quantify gene expression in biopsied tissues in which expression of CCYPR may be correlated with disease. The diagnostic assay may be used to determine absence, presence, and excess expression of CCYPR, and to monitor regulation of CCYPR levels during therapeutic intervention.

In one aspect, hybridization with PCR probes which are capable of detecting polynucleotide

15 sequences, including genomic sequences, encoding CCYPR or closely related molecules may be used to identify nucleic acid sequences which encode CCYPR. The specificity of the probe, whether it is made from a highly specific region, e.g., the 5' regulatory region, or from a less specific region, e.g., a conserved motif, and the stringency of the hybridization or amplification will determine whether the probe identifies only naturally occurring sequences encoding CCYPR, allelic variants, or related

20 sequences.

Probes may also be used for the detection of related sequences, and may have at least 50% sequence identity to any of the CCYPR encoding sequences. The hybridization probes of the subject invention may be DNA or RNA and may be derived from the sequence of SEQ ID NO:55-108 or from genomic sequences including promoters, enhancers, and introns of the CCYPR gene.

Means for producing specific hybridization probes for DNAs encoding CCYPR include the cloning of polynucleotide sequences encoding CCYPR or CCYPR derivatives into vectors for the production of mRNA probes. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes *in vitro* by means of the addition of the appropriate RNA

25 polymerases and the appropriate labeled nucleotides. Hybridization probes may be labeled by a variety of reporter groups, for example, by radionuclides such as ³²P or ³⁵S, or by enzymatic labels, such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems, and the like.

Polynucleotide sequences encoding CCYPR may be used for the diagnosis of disorders associated with expression of CCYPR. Examples of such disorders include, but are not limited to, an immune disorder such as inflammation, actinic keratosis, acquired immunodeficiency syndrome

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- (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, arteriosclerosis, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), bronchitis, bursitis, cholecystitis, cirrhosis, contact dermatitis, Crohn's disease, atopic
- 5 dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, paroxysmal nocturnal hemoglobinuria, hepatitis, hyper eosinophilia, irritable bowel syndrome, mixed connective tissue disorder (MCTD), multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation,
- 10 myelofibrosis, osteoarthritis, osteoporosis, pancreatitis, polycythemia vera, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, primary thrombocythemia, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections,
- 15 trauma, and hematopoietic cancer including lymphoma, leukemia, and myeloma; a developmental disorder such as renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, Duchenne and Becker muscular dystrophy, epilepsy, gonadal dysgenesis, WAGR syndrome (Wilms' tumor, aniridia, genitourinary abnormalities, and mental retardation), Smith-Magenis syndrome, myelodysplastic syndrome, hereditary mucoepithelial dysplasia, hereditary keratodermas, hereditary
- 20 neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Sydenham's chorea and cerebral palsy, spina bifida, anencephaly, craniorachischisis, congenital glaucoma, cataract, sensorineural hearing loss, and disorders of immune cell activation; a cell signaling disorder including endocrine disorders such as disorders of the hypothalamus and pituitary resulting from lesions such as primary brain tumors,
- 25 adenomas, infarction associated with pregnancy, hypophysectomy, aneurysms, vascular malformations, thrombosis, infections, immunological disorders, and complications due to head trauma; disorders associated with hyperpituitarism including acromegaly, gigantism, and syndrome of inappropriate antidiuretic hormone (ADH) secretion (SIADH) often caused by benign adenoma; disorders associated with hypothyroidism including goiter, myxedema, acute thyroiditis associated
- 30 with bacterial infection; disorders associated with hyperparathyroidism including Conn disease (chronic hypercalcemia); pancreatic disorders such as Type I or Type II diabetes mellitus and associated complications; disorders associated with the adrenals such as hyperplasia, carcinoma, or adenoma of the adrenal cortex, hypertension associated with alkalosis; disorders associated with gonadal steroid hormones such as: in women, abnormal prolactin production, infertility, including
- 35 tubal disease, ovulatory defects, and endometriosis, perturbations of the menstrual cycle, polycystic

ovarian disease, ovarian hyperstimulation syndrome, an endometrial or ovarian tumor, a uterine fibroid, autoimmune disorders, an ectopic pregnancy, teratogenesis, hyperprolactinemia, isolated gonadotropin deficiency, amenorrhea, galactorrhea, hermaphroditism, hirsutism and virilization, breast cancer, and fibrocystic breast disease; and, in post-menopausal women, osteoporosis; and, in men, Leydig cell deficiency, male climacteric phase, germinal cell aplasia, hypergonadal disorders associated with Leydig cell tumors, androgen resistance associated with absence of androgen receptors, syndrome of 5 α -reductase, a disruption of spermatogenesis, abnormal sperm physiology, cancer of the testis, cancer of the prostate, benign prostatic hyperplasia, prostatitis, Peyronie's disease, impotence, carcinoma of the male breast, and gynecomastia; and a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus. The polynucleotide sequences encoding CCYPR may be used in Southern or northern analysis, dot blot, or other membrane-based technologies; in PCR technologies; in dipstick, pin, and multiformat ELISA-like assays; and in microarrays utilizing fluids or tissues from patients to detect altered CCYPR expression. Such qualitative or quantitative methods are well known in the art.

In a particular aspect, the nucleotide sequences encoding CCYPR may be useful in assays that detect the presence of associated disorders, particularly those mentioned above. The nucleotide sequences encoding CCYPR may be labeled by standard methods and added to a fluid or tissue sample from a patient under conditions suitable for the formation of hybridization complexes. After a suitable incubation period, the sample is washed and the signal is quantified and compared with a standard value. If the amount of signal in the patient sample is significantly altered in comparison to a control sample then the presence of altered levels of nucleotide sequences encoding CCYPR in the sample indicates the presence of the associated disorder. Such assays may also be used to evaluate the efficacy of a particular therapeutic treatment regimen in animal studies, in clinical trials, or to monitor the treatment of an individual patient.

In order to provide a basis for the diagnosis of a disorder associated with expression of CCYPR, a normal or standard profile for expression is established. This may be accomplished by combining body fluids or cell extracts taken from normal subjects, either animal or human, with a sequence, or a fragment thereof, encoding CCYPR, under conditions suitable for hybridization or amplification. Standard hybridization may be quantified by comparing the values obtained from normal subjects with values from an experiment in which a known amount of a substantially purified

polynucleotide is used. Standard values obtained in this manner may be compared with values obtained from samples from patients who are symptomatic for a disorder. Deviation from standard values is used to establish the presence of a disorder.

Once the presence of a disorder is established and a treatment protocol is initiated, hybridization assays may be repeated on a regular basis to determine if the level of expression in the patient begins to approximate that which is observed in the normal subject. The results obtained from successive assays may be used to show the efficacy of treatment over a period ranging from several days to months.

With respect to cancer, the presence of an abnormal amount of transcript (either under- or overexpressed) in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Additional diagnostic uses for oligonucleotides designed from the sequences encoding CCYPR may involve the use of PCR. These oligomers may be chemically synthesized, generated enzymatically, or produced *in vitro*. Oligomers will preferably contain a fragment of a polynucleotide encoding CCYPR, or a fragment of a polynucleotide complementary to the polynucleotide encoding CCYPR, and will be employed under optimized conditions for identification of a specific gene or condition.

Oligomers may also be employed under less stringent conditions for detection or quantification of closely related DNA or RNA sequences.

In a particular aspect, oligonucleotide primers derived from the polynucleotide sequences encoding CCYPR may be used to detect single nucleotide polymorphisms (SNPs). SNPs are substitutions, insertions and deletions that are a frequent cause of inherited or acquired genetic disease in humans. Methods of SNP detection include, but are not limited to, single-stranded conformation polymorphism (SSCP) and fluorescent SSCP (fSSCP) methods. In SSCP, oligonucleotide primers derived from the polynucleotide sequences encoding CCYPR are used to amplify DNA using the polymerase chain reaction (PCR). The DNA may be derived, for example, from diseased or normal tissue, biopsy samples, bodily fluids, and the like. SNPs in the DNA cause differences in the secondary and tertiary structures of PCR products in single-stranded form, and these differences are detectable using gel electrophoresis in non-denaturing gels. In fSSCP, the oligonucleotide primers are fluorescently labeled, which allows detection of the amplimers in high-throughput equipment such as DNA sequencing machines. Additionally, sequence database analysis methods, termed *in silico* SNP (isSNP), are capable of identifying polymorphisms by comparing the sequence of individual

overlapping DNA fragments which assemble into a common consensus sequence. These computer-based methods filter out sequence variations due to laboratory preparation of DNA and sequencing errors using statistical models and automated analyses of DNA sequence chromatograms. In the alternative, SNPs may be detected and characterized by mass spectrometry using, for example, the high
5 throughput MASSARRAY system (Sequenom, Inc., San Diego CA).

Methods which may also be used to quantify the expression of CCYPR include radiolabeling or biotinylating nucleotides, coamplification of a control nucleic acid, and interpolating results from standard curves. (See, e.g., Melby, P.C. et al. (1993) *J. Immunol. Methods* 159:235-244; Duplaa, C. et al. (1993) *Anal. Biochem.* 212:229-236.) The speed of quantitation of multiple samples may be
10 accelerated by running the assay in a high-throughput format where the oligomer or polynucleotide of interest is presented in various dilutions and a spectrophotometric or colorimetric response gives rapid quantitation.

In further embodiments, oligonucleotides or longer fragments derived from any of the polynucleotide sequences described herein may be used as elements on a microarray. The microarray
15 can be used in transcript imaging techniques which monitor the relative expression levels of large numbers of genes simultaneously as described in Seilhamer, J.J. et al., "Comparative Gene Transcript Analysis," U.S. Patent No. 5,840,484, incorporated herein by reference. The microarray may also be used to identify genetic variants, mutations, and polymorphisms. This information may be used to determine gene function, to understand the genetic basis of a disorder, to diagnose a disorder, to monitor
20 progression/regression of disease as a function of gene expression, and to develop and monitor the activities of therapeutic agents in the treatment of disease. In particular, this information may be used to develop a pharmacogenomic profile of a patient in order to select the most appropriate and effective treatment regimen for that patient. For example, therapeutic agents which are highly effective and display the fewest side effects may be selected for a patient based on his/her pharmacogenomic profile.

25 In another embodiment, antibodies specific for CCYPR, or CCYPR or fragments thereof may be used as elements on a microarray. The microarray may be used to monitor or measure protein-protein interactions, drug-target interactions, and gene expression profiles, as described above.

A particular embodiment relates to the use of the polynucleotides of the present invention to generate a transcript image of a tissue or cell type. A transcript image represents the global pattern of
30 gene expression by a particular tissue or cell type. Global gene expression patterns are analyzed by quantifying the number of expressed genes and their relative abundance under given conditions and at a given time. (See Seilhamer et al., "Comparative Gene Transcript Analysis," U.S. Patent Number 5,840,484, expressly incorporated by reference herein.) Thus a transcript image may be generated by hybridizing the polynucleotides of the present invention or their complements to the totality of

transcripts or reverse transcripts of a particular tissue or cell type. In one embodiment, the hybridization takes place in high-throughput format, wherein the polynucleotides of the present invention or their complements comprise a subset of a plurality of elements on a microarray. The resultant transcript image would provide a profile of gene activity.

Transcript images may be generated using transcripts isolated from tissues, cell lines, biopsies, or other biological samples. The transcript image may thus reflect gene expression in vivo, as in the case of a tissue or biopsy sample, or in vitro, as in the case of a cell line.

Transcript images which profile the expression of the polynucleotides of the present invention may also be used in conjunction with in vitro model systems and preclinical evaluation of pharmaceuticals, as well as toxicological testing of industrial and naturally-occurring environmental compounds. All compounds induce characteristic gene expression patterns, frequently termed molecular fingerprints or toxicant signatures, which are indicative of mechanisms of action and toxicity (Nuwaysir, E.F. et al. (1999) Mol. Carcinog. 24:153-159; Steiner, S. and N.L. Anderson (2000) Toxicol. Lett. 112-113:467-471, expressly incorporated by reference herein). If a test compound has a signature similar to that of a compound with known toxicity, it is likely to share those toxic properties. These fingerprints or signatures are most useful and refined when they contain expression information from a large number of genes and gene families. Ideally, a genome-wide measurement of expression provides the highest quality signature. Even genes whose expression is not altered by any tested compounds are important as well, as the levels of expression of these genes are used to normalize the rest of the expression data. The normalization procedure is useful for comparison of expression data after treatment with different compounds. While the assignment of gene function to elements of a toxicant signature aids in interpretation of toxicity mechanisms, knowledge of gene function is not necessary for the statistical matching of signatures which leads to prediction of toxicity. (See, for example, Press Release 00-02 from the National Institute of Environmental Health Sciences, released February 29, 2000, available at <http://www.niehs.nih.gov/oc/news/toxchip.htm>.) Therefore, it is important and desirable in toxicological screening using toxicant signatures to include all expressed gene sequences.

In one embodiment, the toxicity of a test compound is assessed by treating a biological sample containing nucleic acids with the test compound. Nucleic acids that are expressed in the treated biological sample are hybridized with one or more probes specific to the polynucleotides of the present invention, so that transcript levels corresponding to the polynucleotides of the present invention may be quantified. The transcript levels in the treated biological sample are compared with levels in an untreated biological sample. Differences in the transcript levels between the two samples are indicative of a toxic response caused by the test compound in the treated sample.

Another particular embodiment relates to the use of the polypeptide sequences of the present

invention to analyze the proteome of a tissue or cell type. The term proteome refers to the global pattern of protein expression in a particular tissue or cell type. Each protein component of a proteome can be subjected individually to further analysis. Proteome expression patterns, or profiles, are analyzed by quantifying the number of expressed proteins and their relative abundance under given

5 conditions and at a given time. A profile of a cell's proteome may thus be generated by separating and analyzing the polypeptides of a particular tissue or cell type. In one embodiment, the separation is achieved using two-dimensional gel electrophoresis, in which proteins from a sample are separated by isoelectric focusing in the first dimension, and then according to molecular weight by sodium dodecyl sulfate slab gel electrophoresis in the second dimension (Steiner and Anderson, supra). The proteins are

10 visualized in the gel as discrete and uniquely positioned spots, typically by staining the gel with an agent such as Coomassie Blue or silver or fluorescent stains. The optical density of each protein spot is generally proportional to the level of the protein in the sample. The optical densities of equivalently positioned protein spots from different samples, for example, from biological samples either treated or untreated with a test compound or therapeutic agent, are compared to identify any changes in protein

15 spot density related to the treatment. The proteins in the spots are partially sequenced using, for example, standard methods employing chemical or enzymatic cleavage followed by mass spectrometry. The identity of the protein in a spot may be determined by comparing its partial sequence, preferably of at least 5 contiguous amino acid residues, to the polypeptide sequences of the present invention. In some cases, further sequence data may be obtained for definitive protein identification.

20 A proteomic profile may also be generated using antibodies specific for CCYPR to quantify the levels of CCYPR expression. In one embodiment, the antibodies are used as elements on a microarray, and protein expression levels are quantified by exposing the microarray to the sample and detecting the levels of protein bound to each array element (Lueking, A. et al. (1999) *Anal. Biochem.* 270:103-111; Mendoe, L.G. et al. (1999) *Biotechniques* 27:778-788). Detection may be performed by a variety of

25 methods known in the art, for example, by reacting the proteins in the sample with a thiol- or amino-reactive fluorescent compound and detecting the amount of fluorescence bound at each array element.

Toxicant signatures at the proteome level are also useful for toxicological screening, and should be analyzed in parallel with toxicant signatures at the transcript level. There is a poor correlation between transcript and protein abundances for some proteins in some tissues (Anderson, N.L. and J. Seilhamer (1997) *Electrophoresis* 18:533-537), so proteome toxicant signatures may be useful in the

30 analysis of compounds which do not significantly affect the transcript image, but which alter the proteomic profile. In addition, the analysis of transcripts in body fluids is difficult, due to rapid degradation of mRNA, so proteomic profiling may be more reliable and informative in such cases.

In another embodiment, the toxicity of a test compound is assessed by treating a biological

sample containing proteins with the test compound. Proteins that are expressed in the treated biological sample are separated so that the amount of each protein can be quantified. The amount of each protein is compared to the amount of the corresponding protein in an untreated biological sample. A difference in the amount of protein between the two samples is indicative of a toxic response to the test compound

5 in the treated sample. Individual proteins are identified by sequencing the amino acid residues of the individual proteins and comparing these partial sequences to the polypeptides of the present invention.

In another embodiment, the toxicity of a test compound is assessed by treating a biological sample containing proteins with the test compound. Proteins from the biological sample are incubated with antibodies specific to the polypeptides of the present invention. The amount of protein recognized

10 by the antibodies is quantified. The amount of protein in the treated biological sample is compared with the amount in an untreated biological sample. A difference in the amount of protein between the two samples is indicative of a toxic response to the test compound in the treated sample.

Microarrays may be prepared, used, and analyzed using methods known in the art. (See, e.g., Brennan, T.M. et al. (1995) U.S. Patent No. 5,474,796; Schena, M. et al. (1996) Proc. Natl. Acad. Sci. USA 93:10614-10619; Baldeschweiler et al. (1995) PCT application WO95/251116; Shalon, D. et al. (1995) PCT application WO95/35505; Heller, R.A. et al. (1997) Proc. Natl. Acad. Sci. USA 94:2150-2155; and Heller, M.J. et al. (1997) U.S. Patent No. 5,605,662.) Various types of microarrays are well known and thoroughly described in DNA Microarrays: A Practical Approach, M. Schena, ed. (1999) Oxford University Press, London, hereby expressly incorporated by reference.

15

In another embodiment of the invention, nucleic acid sequences encoding CCYPR may be used to generate hybridization probes useful in mapping the naturally occurring genomic sequence. Either coding or noncoding sequences may be used, and in some instances, noncoding sequences may be preferable over coding sequences. For example, conservation of a coding sequence among members of a multi-gene family may potentially cause undesired cross hybridization during chromosomal

25 mapping. The sequences may be mapped to a particular chromosome, to a specific region of a chromosome, or to artificial chromosome constructions, e.g., human artificial chromosomes (HACs), yeast artificial chromosomes (YACs), bacterial artificial chromosomes (BACs), bacterial P1 constructions, or single chromosome cDNA libraries. (See, e.g., Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355; Price, C.M. (1993) Blood Rev. 7:127-134; and Trask, B.J. (1991) Trends Genet. 7:149-154.) Once mapped, the nucleic acid sequences of the invention may be used to develop genetic linkage maps, for example, which correlate the inheritance of a disease state with the inheritance of a particular chromosome region or restriction fragment length polymorphism (RFLP). (See, e.g., Lander, E.S. and D. Botstein (1986) Proc. Natl. Acad. Sci. USA 83:7353-7357.)

30

Fluorescent in situ hybridization (FISH) may be correlated with other physical and genetic map

35 data. (See, e.g., Heinz-Ulrich, et al. (1995) in Meyers, supra, pp. 965-968.) Examples of genetic map

data can be found in various scientific journals or at the Online Mendelian Inheritance in Man (OMIM) World Wide Web site. Correlation between the location of the gene encoding CCYPR on a physical map and a specific disorder, or a predisposition to a specific disorder, may help define the region of DNA associated with that disorder and thus may further positional cloning efforts.

5 In situ hybridization of chromosomal preparations and physical mapping techniques, such as linkage analysis using established chromosomal markers, may be used for extending genetic maps. Often the placement of a gene on the chromosome of another mammalian species, such as mouse, may reveal associated markers even if the exact chromosomal locus is not known. This information is valuable to investigators searching for disease genes using positional cloning or other gene discovery
10 techniques. Once the gene or genes responsible for a disease or syndrome have been crudely localized by genetic linkage to a particular genomic region, e.g., ataxia-telangiectasia to 11q22-23, any sequences mapping to that area may represent associated or regulatory genes for further investigation. (See, e.g., Gatti, R.A. et al. (1988) Nature 336:577-580.) The nucleotide sequence of the instant invention may also be used to detect differences in the chromosomal location due to translocation, inversion, etc.,
15 among normal, carrier, or affected individuals.

In another embodiment of the invention, CCYPR, its catalytic or immunogenic fragments, or oligopeptides thereof can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. The formation of binding complexes
20 between CCYPR and the agent being tested may be measured.

Another technique for drug screening provides for high throughput screening of compounds having suitable binding affinity to the protein of interest. (See, e.g., Geysen, et al. (1984) PCT application WO84/03564.) In this method, large numbers of different small test compounds are synthesized on a solid substrate. The test compounds are reacted with CCYPR, or fragments thereof,
25 and washed. Bound CCYPR is then detected by methods well known in the art. Purified CCYPR can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

In another embodiment, one may use competitive drug screening assays in which neutralizing
30 antibodies capable of binding CCYPR specifically compete with a test compound for binding CCYPR. In this manner, antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with CCYPR.

In additional embodiments, the nucleotide sequences which encode CCYPR may be used in any molecular biology techniques that have yet to be developed, provided the new techniques rely on

properties of nucleotide sequences that are currently known, including, but not limited to, such properties as the triplet genetic code and specific base pair interactions.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific
 5 embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

The disclosures of all patents, applications, and publications mentioned above and below, in particular U.S. Ser. No. 60/145,075, U.S. Ser. No. 60/153,129, and U.S. Ser. No. 60/164,647, are hereby expressly incorporated by reference.

10

EXAMPLES

I. Construction of cDNA Libraries

RNA was purchased from Clontech or isolated from tissues described in Table 4. Some tissues were homogenized and lysed in guanidinium isothiocyanate, while others were homogenized and lysed
 15 in phenol or in a suitable mixture of denaturants, such as TRIZOL (Life Technologies), a monophasic solution of phenol and guanidine isothiocyanate. The resulting lysates were centrifuged over CsCl cushions or extracted with chloroform. RNA was precipitated from the lysates with either isopropanol or sodium acetate and ethanol, or by other routine methods.

Phenol extraction and precipitation of RNA were repeated as necessary to increase RNA
 20 purity. In some cases, RNA was treated with DNase. For most libraries, poly(A+) RNA was isolated using oligo d(T)-coupled paramagnetic particles (Promega), OLIGOTEX latex particles (QIAGEN, Chatsworth CA), or an OLIGOTEX mRNA purification kit (QIAGEN). Alternatively, RNA was isolated directly from tissue lysates using other RNA isolation kits, e.g., the POLY(A)PURE mRNA purification kit (Ambion, Austin TX).

In some cases, Stratagene was provided with RNA and constructed the corresponding cDNA
 25 libraries. Otherwise, cDNA was synthesized and cDNA libraries were constructed with the UNIZAP vector system (Stratagene) or SUPERScript plasmid system (Life Technologies), using the recommended procedures or similar methods known in the art. (See, e.g., Ausubel, 1997, supra, units 5.1-6.6.) Reverse transcription was initiated using oligo d(T) or random primers. Synthetic
 30 oligonucleotide adapters were ligated to double stranded cDNA, and the cDNA was digested with the appropriate restriction enzyme or enzymes. For most libraries, the cDNA was size-selected (300-1000 bp) using SEPHACRYL S1000, SEPHAROSE CL2B, or SEPHAROSE CL4B column chromatography (Amersham Pharmacia Biotech) or preparative agarose gel electrophoresis. cDNAs were ligated into compatible restriction enzyme sites of the polylinker of a suitable plasmid, e.g.,
 35 PBLUESCRIPT plasmid (Stratagene), PSPORT1 plasmid (Life Technologies), pCDNA2.1 plasmid

(Invitrogen, Carlsbad CA), or pINCY plasmid (Incyte Genomics, Palo Alto CA). Recombinant plasmids were transformed into competent *E. coli* cells including XL1-Blue, XL1-BlueMRF, or SOLR from Stratagene or DH5 α , DH10B, or ElectroMAX DH10B from Life Technologies.

II. Isolation of cDNA Clones

Plasmids obtained as described in Example I were recovered from host cells by *in vivo* excision using the UNIZAP vector system (Stratagene) or by cell lysis. Plasmids were purified using at least one of the following: a Magic or WIZARD Minipreps DNA purification system (Promega); an AGTC Miniprep purification kit (Edge Biosystems, Gaithersburg MD); and QIAWELL 8 Plasmid, QIAWELL 8 Plus Plasmid, QIAWELL 8 Ultra Plasmid purification systems or the R.E.A.L. PREP 96 plasmid purification kit from QIAGEN. Following precipitation, plasmids were resuspended in 0.1 ml of distilled water and stored, with or without lyophilization, at 4°C.

Alternatively, plasmid DNA was amplified from host cell lysates using direct link PCR in a high-throughput format (Rao, V.B. (1994) Anal. Biochem. 216:1-14). Host cell lysis and thermal cycling steps were carried out in a single reaction mixture. Samples were processed and stored in 384-well plates, and the concentration of amplified plasmid DNA was quantified fluorometrically using PICOGREEN dye (Molecular Probes, Eugene OR) and a FLUOROSKAN II fluorescence scanner (Labsystems Oy, Helsinki, Finland).

III. Sequencing and Analysis

Incyte cDNA recovered in plasmids as described in Example II were sequenced as follows.

Sequencing reactions were processed using standard methods or high-throughput instrumentation such as the ABI CATALYST 800 (PE Biosystems) thermal cycler or the PTC-200 thermal cycler (MJ Research) in conjunction with the HYDRA microdispenser (Robbins Scientific) or the MICROLAB 2200 (Hamilton) liquid transfer system. cDNA sequencing reactions were prepared using reagents provided by Amersham Pharmacia Biotech or supplied in ABI sequencing kits such as the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (PE Biosystems). Electrophoretic separation of cDNA sequencing reactions and detection of labeled polynucleotides were carried out using the MEGABACE 1000 DNA sequencing system (Molecular Dynamics); the ABI PRISM 373 or 377 sequencing system (PE Biosystems) in conjunction with standard ABI protocols and base calling software; or other sequence analysis systems known in the art. Reading frames within the cDNA sequences were identified using standard methods (reviewed in Ausubel, 1997, *supra*, unit 7.7). Some of the cDNA sequences were selected for extension using the techniques disclosed in Example VI.

The polynucleotide sequences derived from cDNA sequencing were assembled and analyzed using a combination of software programs which utilize algorithms well known to those skilled in the art. Table 5 summarizes the tools, programs, and algorithms used and provides applicable descriptions,

references, and threshold parameters. The first column of Table 5 shows the tools, programs, and algorithms used, the second column provides brief descriptions thereof, the third column presents appropriate references, all of which are incorporated by reference herein in their entirety, and the fourth column presents, where applicable, the scores, probability values, and other parameters used to evaluate the strength of a match between two sequences (the higher the score, the greater the homology between two sequences). Sequences were analyzed using MACDNASIS PRO software (Hitachi Software Engineering, South San Francisco CA) and LASERGENE software (DNASTAR). Polynucleotide and polypeptide sequence alignments were generated using the default parameters specified by the clustal algorithm as incorporated into the MEGALIGN multisequence alignment program (DNASTAR), which also calculates the percent identity between aligned sequences.

The polynucleotide sequences were validated by removing vector, linker, and polyA sequences and by masking ambiguous bases, using algorithms and programs based on BLAST, dynamic programming, and dinucleotide nearest neighbor analysis. The sequences were then queried against a selection of public databases such as the GenBank primate, rodent, mammalian, vertebrate, and eukaryote databases, and BLOCKS, PRINTS, DOMO, PRODOM, and PFAM to acquire annotation using programs based on BLAST, FASTA, and BLIMPS. The sequences were assembled into full length polynucleotide sequences using programs based on Phred, Phrap, and Consed, and were screened for open reading frames using programs based on GeneMark, BLAST, and FASTA. The full length polynucleotide sequences were translated to derive the corresponding full length amino acid sequences, and these full length sequences were subsequently analyzed by querying against databases such as the GenBank databases (described above), SwissProt, BLOCKS, PRINTS, DOMO, PRODOM, Prosite, and Hidden Markov Model (HMM)-based protein family databases such as PFAM. HMM is a probabilistic approach which analyzes consensus primary structures of gene families. (See, e.g., Eddy, S.R. (1996) *Curr. Opin. Struct. Biol.* 6:361-365.)

The programs described above for the assembly and analysis of full length polynucleotide and amino acid sequences were also used to identify polynucleotide sequence fragments from SEQ ID NO:55-108. Fragments from about 20 to about 4000 nucleotides which are useful in hybridization and amplification technologies were described in The Invention section above.

IV. Analysis of Polynucleotide Expression

Northern analysis is a laboratory technique used to detect the presence of a transcript of a gene and involves the hybridization of a labeled nucleotide sequence to a membrane on which RNAs from a particular cell type or tissue have been bound. (See, e.g., Sambrook, supra, ch. 7; Ausubel, 1995, supra, ch. 4 and 16.)

Analogous computer techniques applying BLAST were used to search for identical or related

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molecules in cDNA databases such as GenBank or LIFESEQ (Incyte Genomics). This analysis is much faster than multiple membrane-based hybridizations. In addition, the sensitivity of the computer search can be modified to determine whether any particular match is categorized as exact or similar.

The basis of the search is the product score, which is defined as:

$$5 \quad \frac{\text{BLAST Score} \times \text{Percent Identity}}{5 \times \text{minimum \{length(Seq. 1), length(Seq. 2)\}}}$$

The product score takes into account both the degree of similarity between two sequences and the length of the sequence match. The product score is a normalized value between 0 and 100, and is calculated as follows: the BLAST score is multiplied by the percent nucleotide identity and the product is divided by (5 times the length of the shorter of the two sequences). The BLAST score is calculated by assigning a score of +5 for every base that matches in a high-scoring segment pair (HSP), and -4 for every mismatch. Two sequences may share more than one HSP (separated by gaps). If there is more than one HSP, then the pair with the highest BLAST score is used to calculate the product score. The product score represents a balance between fractional overlap and quality in a BLAST alignment. For example, a product score of 100 is produced only for 100% identity over the entire length of the shorter of the two sequences being compared. A product score of 70 is produced either by 100% identity and 70% overlap at one end, or by 88% identity and 100% overlap at the other. A product score of 50 is produced either by 100% identity and 50% overlap at one end, or 79% identity and 100% overlap.

The results of northern analyses are reported as a percentage distribution of libraries in which the transcript encoding CCYPR occurred. Analysis involved the categorization of cDNA libraries by organ/tissue and disease. The organ/tissue categories included cardiovascular, dermatologic, developmental, endocrine, gastrointestinal, hematopoietic/immune, musculoskeletal, nervous, reproductive, and urologic. The disease/condition categories included cancer, inflammation, trauma, cell proliferation, neurological, and pooled. For each category, the number of libraries expressing the sequence of interest was counted and divided by the total number of libraries across all categories. Percentage values of tissue-specific and disease- or condition-specific expression are reported in Table 3.

V. Chromosomal Mapping of CCYPR Encoding Polynucleotides

The cDNA sequences which were used to assemble SEQ ID NO:55-108 were compared with sequences from the Incyte LIFESEQ database and public domain databases using BLAST and other implementations of the Smith-Waterman algorithm. Sequences from these databases that matched SEQ ID NO:55-108 were assembled into clusters of contiguous and overlapping sequences using assembly algorithms such as Phrap (Table 5). Radiation hybrid and genetic mapping data available

from public resources such as the Stanford Human Genome Center (SHGC), Whitehead Institute for Genome Research (WIGR), and Généthon were used to determine if any of the clustered sequences had been previously mapped. Inclusion of a mapped sequence in a cluster resulted in the assignment of all sequences of that cluster, including its particular SEQ ID NO., to that map location.

The genetic map locations of SEQ ID NO:61, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:81, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:104, and SEQ ID NO:105 are described in The Invention as ranges, or intervals, of human chromosomes. More than one map location is reported for SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:90, and SEQ ID NO:100, indicating that previously mapped sequences having similarity, but not complete identity, to SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:90, and SEQ ID NO:100 were assembled into their respective clusters. The map position of an interval, in centiMorgans, is measured relative to the terminus of the chromosome's p-arm. (The centiMorgan (cM) is a unit of measurement based on recombination frequencies between chromosomal markers. On average, 1 cM is roughly equivalent to 1 megabase (Mb) of DNA in humans, although this can vary widely due to hot and cold spots of recombination.) The cM distances are based on genetic markers mapped by Généthon which provide boundaries for radiation hybrid markers whose sequences were included in each of the clusters. Human genome maps and other resources available to the public, such as the NCBI "GeneMap'99" World Wide Web site (<http://www.ncbi.nlm.nih.gov/genemap/>), can be employed to determine if previously identified disease genes map within or in proximity to the intervals indicated above.

VI. Extension of CCYPR Encoding Polynucleotides

The full length nucleic acid sequences of SEQ ID NO:55-108 were produced by extension of an appropriate fragment of the full length molecule using oligonucleotide primers designed from this fragment. One primer was synthesized to initiate 5' extension of the known fragment, and the other primer, to initiate 3' extension of the known fragment. The initial primers were designed using OLIGO 4.06 software (National Biosciences), or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the target sequence at temperatures of about 68°C to about 72°C. Any stretch of nucleotides which would result in hairpin structures and primer-primer dimerizations was avoided.

Selected human cDNA libraries were used to extend the sequence. If more than one extension was necessary or desired, additional or nested sets of primers were designed.

High fidelity amplification was obtained by PCR using methods well known in the art. PCR was performed in 96-well plates using the PTC-200 thermal cycler (MJ Research, Inc.). The reaction mix contained DNA template, 200 nmol of each primer, reaction buffer containing Mg^{2+} , $(NH_4)_2SO_4$, and β -mercaptoethanol, Taq DNA polymerase (Amersham Pharmacia Biotech), ELONGASE enzyme

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(Life Technologies), and Pfu DNA polymerase (Stratagene), with the following parameters for primer pair PCI A and PCI B: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C. In the alternative, the parameters for primer pair T7 and SK+ were as follows: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 57°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C.

The concentration of DNA in each well was determined by dispensing 100 µl PICOGREEN quantitation reagent (0.25% (v/v) PICOGREEN; Molecular Probes, Eugene OR) dissolved in 1X TE and 0.5 µl of undiluted PCR product into each well of an opaque fluorimeter plate (Corning Costar, Acton MA), allowing the DNA to bind to the reagent. The plate was scanned in a Fluoroskan II (Labsystems Oy, Helsinki, Finland) to measure the fluorescence of the sample and to quantify the concentration of DNA. A 5 µl to 10 µl aliquot of the reaction mixture was analyzed by electrophoresis on a 1 % agarose mini-gel to determine which reactions were successful in extending the sequence.

The extended nucleotides were desalted and concentrated, transferred to 384-well plates, digested with CviJI cholera virus endonuclease (Molecular Biology Research, Madison WI), and sonicated or sheared prior to religation into pUC 18 vector (Amersham Pharmacia Biotech). For shotgun sequencing, the digested nucleotides were separated on low concentration (0.6 to 0.8%) agarose gels, fragments were excised, and agar digested with Agar ACE (Promega). Extended clones were religated using T4 ligase (New England Biolabs, Beverly MA) into pUC 18 vector (Amersham Pharmacia Biotech), treated with Pfu DNA polymerase (Stratagene) to fill-in restriction site overhangs, and transfected into competent *E. coli* cells. Transformed cells were selected on antibiotic-containing media, and individual colonies were picked and cultured overnight at 37°C in 384-well plates in LB/2x carb liquid media.

The cells were lysed, and DNA was amplified by PCR using Taq DNA polymerase (Amersham Pharmacia Biotech) and Pfu DNA polymerase (Stratagene) with the following parameters: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 72°C, 2 min; Step 5: steps 2, 3, and 4 repeated 29 times; Step 6: 72°C, 5 min; Step 7: storage at 4°C. DNA was quantified by PICOGREEN reagent (Molecular Probes) as described above. Samples with low DNA recoveries were reamplified using the same conditions as described above. Samples were diluted with 20% dimethylsulfoxide (1:2, v/v), and sequenced using DYENAMIC energy transfer sequencing primers and the DYENAMIC DIRECT kit (Amersham Pharmacia Biotech) or the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (PE Biosystems).

In like manner, the polynucleotide sequences of SEQ ID NO:55-108 are used to obtain 5' regulatory sequences using the procedure above, along with oligonucleotides designed for such

extension, and an appropriate genomic library.

VII. Labeling and Use of Individual Hybridization Probes

Hybridization probes derived from SEQ ID NO:55-108 are employed to screen cDNAs, genomic DNAs, or mRNAs. Although the labeling of oligonucleotides, consisting of about 20 base pairs, is specifically described, essentially the same procedure is used with larger nucleotide fragments. Oligonucleotides are designed using state-of-the-art software such as OLIGO 4.06 software (National Biosciences) and labeled by combining 50 pmol of each oligomer, 250 μ Ci of [γ - 32 P] adenosine triphosphate (Amersham Pharmacia Biotech), and T4 polynucleotide kinase (DuPont NEN, Boston MA). The labeled oligonucleotides are substantially purified using a SEPHADEX G-25 superfine size exclusion dextran bead column (Amersham Pharmacia Biotech). An aliquot containing 10^7 counts per minute of the labeled probe is used in a typical membrane-based hybridization analysis of human genomic DNA digested with one of the following endonucleases: Ase I, Bgl II, Eco RI, Pst I, Xba I, or Pvu II (DuPont NEN).

The DNA from each digest is fractionated on a 0.7% agarose gel and transferred to nylon membranes (Nytran Plus, Schleicher & Schuell, Durham NH). Hybridization is carried out for 16 hours at 40°C. To remove nonspecific signals, blots are sequentially washed at room temperature under conditions of up to, for example, 0.1 x saline sodium citrate and 0.5% sodium dodecyl sulfate. Hybridization patterns are visualized using autoradiography or an alternative imaging means and compared.

VIII. Microarrays

The linkage or synthesis of array elements upon a microarray can be achieved utilizing photolithography, piezoelectric printing (ink-jet printing, See, e.g., Baldeschweiler, *supra*), mechanical microspotting technologies, and derivatives thereof. The substrate in each of the aforementioned technologies should be uniform and solid with a non-porous surface (Schna (1999), *supra*). Suggested substrates include silicon, silica, glass slides, glass chips, and silicon wafers. Alternatively, a procedure analogous to a dot or slot blot may also be used to arrange and link elements to the surface of a substrate using thermal, UV, chemical, or mechanical bonding procedures. A typical array may be produced using available methods and machines well known to those of ordinary skill in the art and may contain any appropriate number of elements. (See, e.g., Schna, M. et al. (1995) *Science* 270:467-470; Shalon, D. et al. (1996) *Genome Res.* 6:639-645; Marshall, A. and J. Hodgson (1998) *Nat. Biotechnol.* 16:27-31.)

Full length cDNAs, Expressed Sequence Tags (ESTs), or fragments or oligomers thereof may comprise the elements of the microarray. Fragments or oligomers suitable for hybridization can be selected using software well known in the art such as LASERGENE software (DNASTAR). The array

elements are hybridized with polynucleotides in a biological sample. The polynucleotides in the biological sample are conjugated to a fluorescent label or other molecular tag for ease of detection. After hybridization, nonhybridized nucleotides from the biological sample are removed, and a fluorescence scanner is used to detect hybridization at each array element. Alternatively, laser desorption and mass spectrometry may be used for detection of hybridization. The degree of complementarity and the relative abundance of each polynucleotide which hybridizes to an element on the microarray may be assessed. In one embodiment, microarray preparation and usage is described in detail below.

Tissue or Cell Sample Preparation

Total RNA is isolated from tissue samples using the guanidinium thiocyanate method and poly(A)⁺ RNA is purified using the oligo-(dT) cellulose method. Each poly(A)⁺ RNA sample is reverse transcribed using MMLV reverse-transcriptase, 0.05 pg/ μ l oligo-(dT) primer (21mer), 1X first strand buffer, 0.03 units/ μ l RNase inhibitor, 500 μ M dATP, 500 μ M dGTP, 500 μ M dTTP, 40 μ M dCTP, 40 μ M dCTP-Cy3 (BDS) or dCTP-Cy5 (Amersham Pharmacia Biotech). The reverse transcription reaction is performed in a 25 ml volume containing 200 ng poly(A)⁺ RNA with GEMBRIGHT kits (Incyte). Specific control poly(A)⁺ RNAs are synthesized by in vitro transcription from non-coding yeast genomic DNA. After incubation at 37°C for 2 hr, each reaction sample (one with Cy3 and another with Cy5 labeling) is treated with 2.5 ml of 0.5M sodium hydroxide and incubated for 20 minutes at 85°C to stop the reaction and degrade the RNA. Samples are purified using two successive CHROMA SPIN 30 gel filtration spin columns (CLONTECH Laboratories, Inc. (CLONTECH), Palo Alto CA) and after combining, both reaction samples are ethanol precipitated using 1 ml of glycogen (1 mg/ml), 60 ml sodium acetate, and 300 ml of 100% ethanol. The sample is then dried to completion using a SpeedVAC (Savant Instruments Inc., Holbrook NY) and resuspended in 14 μ l 5X SSC/0.2% SDS.

Microarray Preparation

Sequences of the present invention are used to generate array elements. Each array element is amplified from bacterial cells containing vectors with cloned cDNA inserts. PCR amplification uses primers complementary to the vector sequences flanking the cDNA insert. Array elements are amplified in thirty cycles of PCR from an initial quantity of 1-2 ng to a final quantity greater than 5 μ g. Amplified array elements are then purified using SEPHACRYL-400 (Amersham Pharmacia Biotech).

Purified array elements are immobilized on polymer-coated glass slides. Glass microscope slides (Corning) are cleaned by ultrasound in 0.1% SDS and acetone, with extensive distilled water washes between and after treatments. Glass slides are etched in 4% hydrofluoric acid (VWR Scientific Products Corporation (VWR), West Chester PA), washed extensively in distilled water, and

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coated with 0.05 % aminopropyl silane (Sigma) in 95 % ethanol. Coated slides are cured in a 110°C oven.

Array elements are applied to the coated glass substrate using a procedure described in US Patent No. 5,807,522, incorporated herein by reference. 1 µl of the array element DNA, at an average concentration of 100 ng/µl, is loaded into the open capillary printing element by a high-speed robotic apparatus. The apparatus then deposits about 5 nl of array element sample per slide.

Microarrays are UV-crosslinked using a STRATALINKER UV-crosslinker (Stratagene). Microarrays are washed at room temperature once in 0.2% SDS and three times in distilled water. Non-specific binding sites are blocked by incubation of microarrays in 0.2% casein in phosphate buffered saline (PBS) (Tropix, Inc., Bedford MA) for 30 minutes at 60 °C followed by washes in 0.2% SDS and distilled water as before.

Hybridization

Hybridization reactions contain 9 µl of sample mixture consisting of 0.2 µg each of Cy3 and Cy5 labeled cDNA synthesis products in 5X SSC, 0.2% SDS hybridization buffer. The sample mixture is heated to 65 °C for 5 minutes and is aliquoted onto the microarray surface and covered with an 1.8 cm² coverslip. The arrays are transferred to a waterproof chamber having a cavity just slightly larger than a microscope slide. The chamber is kept at 100% humidity internally by the addition of 140 µl of 5X SSC in a corner of the chamber. The chamber containing the arrays is incubated for about 6.5 hours at 60 °C. The arrays are washed for 10 min at 45 °C in a first wash buffer (1X SSC, 0.1% SDS), three times for 10 minutes each at 45 °C in a second wash buffer (0.1X SSC), and dried.

Detection

Reporter-labeled hybridization complexes are detected with a microscope equipped with an Innova 70 mixed gas 10 W laser (Coherent, Inc., Santa Clara CA) capable of generating spectral lines at 488 nm for excitation of Cy3 and at 632 nm for excitation of Cy5. The excitation laser light is focused on the array using a 20X microscope objective (Nikon, Inc., Melville NY). The slide containing the array is placed on a computer-controlled X-Y stage on the microscope and raster-scanned past the objective. The 1.8 cm x 1.8 cm array used in the present example is scanned with a resolution of 20 micrometers.

In two separate scans, a mixed gas multiline laser excites the two fluorophores sequentially. Emitted light is split, based on wavelength, into two photomultiplier tube detectors (PMT R1477, Hamamatsu Photonics Systems, Bridgewater NJ) corresponding to the two fluorophores. Appropriate filters positioned between the array and the photomultiplier tubes are used to filter the signals. The emission maxima of the fluorophores used are 565 nm for Cy3 and 650 nm for Cy5. Each array is typically scanned twice, one scan per fluorophore using the appropriate filters at the laser source, although the apparatus is capable of recording the spectra from both fluorophores simultaneously.

The sensitivity of the scans is typically calibrated using the signal intensity generated by a cDNA control species added to the sample mixture at a known concentration. A specific location on the array contains a complementary DNA sequence, allowing the intensity of the signal at that location to be correlated with a weight ratio of hybridizing species of 1:100,000. When two samples from different sources (e.g., representing test and control cells), each labeled with a different fluorophore, are hybridized to a single array for the purpose of identifying genes that are differentially expressed, the calibration is done by labeling samples of the calibrating cDNA with the two fluorophores and adding identical amounts of each to the hybridization mixture.

The output of the photomultiplier tube is digitized using a 12-bit RTI-835H analog-to-digital (A/D) conversion board (Analog Devices, Inc., Norwood MA) installed in an IBM-compatible PC computer. The digitized data are displayed as an image where the signal intensity is mapped using a linear 20-color transformation to a pseudocolor scale ranging from blue (low signal) to red (high signal). The data is also analyzed quantitatively. Where two different fluorophores are excited and measured simultaneously, the data are first corrected for optical crosstalk (due to overlapping emission spectra) between the fluorophores using each fluorophore's emission spectrum.

A grid is superimposed over the fluorescence signal image such that the signal from each spot is centered in each element of the grid. The fluorescence signal within each element is then integrated to obtain a numerical value corresponding to the average intensity of the signal. The software used for signal analysis is the GEMTOOLS gene expression analysis program (Incyte).

IX. Complementary Polynucleotides

Sequences complementary to the CCYPR-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring CCYPR. Although use of oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using OLIGO 4.06 software (National Biosciences) and the coding sequence of CCYPR. To inhibit transcription, a complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to the CCYPR-encoding transcript.

X. Expression of CCYPR

Expression and purification of CCYPR is achieved using bacterial or virus-based expression systems. For expression of CCYPR in bacteria, cDNA is subcloned into an appropriate vector containing an antibiotic resistance gene and an inducible promoter that directs high levels of cDNA transcription. Examples of such promoters include, but are not limited to, the *trp-lac* (*lac*) hybrid promoter and the T5 or T7 bacteriophage promoter in conjunction with the *lac* operator regulatory element. Recombinant vectors are transformed into suitable bacterial hosts, e.g., BL21(DE3).

Antibiotic resistant bacteria express CCYPR upon induction with isopropyl beta-D-thiogalactopyranoside (IPTG). Expression of CCYPR in eukaryotic cells is achieved by infecting insect or mammalian cell lines with recombinant Autographica californica nuclear polyhedrosis virus (AcMNPV), commonly known as baculovirus. The nonessential polyhedrin gene of baculovirus is replaced with cDNA encoding CCYPR by either homologous recombination or bacterial-mediated transposition involving transfer plasmid intermediates. Viral infectivity is maintained and the strong polyhedrin promoter drives high levels of cDNA transcription. Recombinant baculovirus is used to infect Spodoptera frugiperda (Sf9) insect cells in most cases, or human hepatocytes, in some cases. Infection of the latter requires additional genetic modifications to baculovirus. (See Engelhard, E.K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945.)

In most expression systems, CCYPR is synthesized as a fusion protein with, e.g., glutathione S-transferase (GST) or a peptide epitope tag, such as FLAG or 6-His, permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates. GST, a 26-kilodalton enzyme from Schistosoma japonicum, enables the purification of fusion proteins on immobilized glutathione under conditions that maintain protein activity and antigenicity (Amersham Pharmacia Biotech). Following purification, the GST moiety can be proteolytically cleaved from CCYPR at specifically engineered sites. FLAG, an 8-amino acid peptide, enables immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies (Eastman Kodak). His, a stretch of six consecutive histidine residues, enables purification on metal-chelate resins (QIAGEN). Methods for protein expression and purification are discussed in Ausubel (1995, supra, ch. 10 and 16). Purified CCYPR obtained by these methods can be used directly in the assays shown in Examples XI and XV.

XI. Demonstration of CCYPR Activity

An assay for CCYPR activity measures cell proliferation as the amount of newly initiated DNA synthesis in Swiss mouse 3T3 cells. A plasmid containing polynucleotides encoding CCYPR is transfected into quiescent 3T3 cultured cells using methods well known in the art. The transiently transfected cells are then incubated in the presence of [³H]thymidine, a radioactive DNA precursor. Where applicable, varying amounts of CCYPR ligand are added to the transfected cells. Incorporation of [³H]thymidine into acid-precipitable DNA is measured over an appropriate time interval, and the amount incorporated is directly proportional to the amount of newly synthesized DNA and CCYPR activity.

XII. Functional Assays

CCYPR function is assessed by expressing the sequences encoding CCYPR at physiologically

elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives high levels of cDNA expression. Vectors of choice include pCMV SPORT plasmid (Life Technologies) and pCR3.1 plasmid (Invitrogen), both of which contain the cytomegalovirus promoter. 5-10 μ g of recombinant vector are transiently transfected into a human cell line, for example, an endothelial or hematopoietic cell line, using either liposome formulations or electroporation. 1-2 μ g of an additional plasmid containing sequences encoding a marker protein are co-transfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP and to evaluate the apoptotic state of the cells and other cellular properties. FCM detects and quantifies the uptake of fluorescent molecules that diagnose events preceding or coincident with cell death. These events include changes in nuclear DNA content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are discussed in Ormerod, M.G. (1994) Flow Cytometry, Oxford, New York NY.

The influence of CCYPR on gene expression can be assessed using highly purified populations of cells transfected with sequences encoding CCYPR and either CD64 or CD64-GFP. CD64 and CD64-GFP are expressed on the surface of transfected cells and bind to conserved regions of human immunoglobulin G (IgG). Transfected cells are efficiently separated from nontransfected cells using magnetic beads coated with either human IgG or antibody against CD64 (DYNAL, Lake Success NY). mRNA can be purified from the cells using methods well known by those of skill in the art. Expression of mRNA encoding CCYPR and other genes of interest can be analyzed by northern analysis or microarray techniques.

XIII. Production of CCYPR Specific Antibodies

CCYPR substantially purified using polyacrylamide gel electrophoresis (PAGE; see, e.g., Harrington, M.G. (1990) *Methods Enzymol.* 182:488-495), or other purification techniques, is used to immunize rabbits and to produce antibodies using standard protocols.

Alternatively, the CCYPR amino acid sequence is analyzed using LASERGENE software (DNASTAR) to determine regions of high immunogenicity, and a corresponding oligopeptide is

synthesized and used to raise antibodies by means known to those of skill in the art. Methods for selection of appropriate epitopes, such as those near the C-terminus or in hydrophilic regions are well described in the art. (See, e.g., Ausubel, 1995, supra, ch. 11.)

Typically, oligopeptides of about 15 residues in length are synthesized using an ABI 431A peptide synthesizer (PE Biosystems) using Fmoc chemistry and coupled to KLH (Sigma-Aldrich, St. Louis MO) by reaction with N-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) to increase immunogenicity. (See, e.g., Ausubel, 1995, supra.) Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. Resulting antisera are tested for antipeptide and anti-CCYPR activity by, for example, binding the peptide or CCYPR to a substrate, blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radio-iodinated goat anti-rabbit IgG.

XIV. Purification of Naturally Occurring CCYPR Using Specific Antibodies

Naturally occurring or recombinant CCYPR is substantially purified by immunoaffinity chromatography using antibodies specific for CCYPR. An immunoaffinity column is constructed by covalently coupling anti-CCYPR antibody to an activated chromatographic resin, such as CNBr-activated SEPHAROSE (Amersham Pharmacia Biotech). After the coupling, the resin is blocked and washed according to the manufacturer's instructions.

Media containing CCYPR are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of CCYPR (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt antibody/CCYPR binding (e.g., a buffer of pH 2 to pH 3, or a high concentration of a chaotrope, such as urea or thiocyanate ion), and CCYPR is collected.

XV. Identification of Molecules Which Interact with CCYPR

CCYPR, or biologically active fragments thereof, are labeled with ¹²⁵I Bolton-Hunter reagent. (See, e.g., Bolton A.E. and W.M. Hunter (1973) *Biochem. J.* 133:529-539.) Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled CCYPR, washed, and any wells with labeled CCYPR complex are assayed. Data obtained using different concentrations of CCYPR are used to calculate values for the number, affinity, and association of CCYPR with the candidate molecules.

Alternatively, molecules interacting with CCYPR are analyzed using the yeast two-hybrid system as described in Fields, S. and O. Song (1989, *Nature* 340:245-246), or using commercially available kits based on the two-hybrid system, such as the MATCHMAKER system (Clontech).

CCYPR may also be used in the PATHCALLING process (CuraGen Corp., New Haven CT) which employs the yeast two-hybrid system in a high-throughput manner to determine all interactions between the proteins encoded by two large libraries of genes (Nandabalan, K. et al. (2000) U.S. Patent

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No. 6,057,101).

Various modifications and variations of the described methods and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention.

- 5 Although the invention has been described in connection with certain embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in molecular biology or related fields are intended to be within the scope of the following claims.

3.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0 15.0 16.0 17.0 18.0 19.0 20.0 21.0 22.0 23.0 24.0 25.0 26.0 27.0 28.0 29.0 30.0 31.0 32.0 33.0 34.0 35.0 36.0 37.0 38.0 39.0 40.0 41.0 42.0 43.0 44.0 45.0 46.0 47.0 48.0 49.0 50.0 51.0 52.0 53.0 54.0 55.0 56.0 57.0 58.0 59.0 60.0 61.0 62.0 63.0 64.0 65.0 66.0 67.0 68.0 69.0 70.0 71.0 72.0 73.0 74.0 75.0 76.0 77.0 78.0 79.0 80.0 81.0 82.0 83.0 84.0 85.0 86.0 87.0 88.0 89.0 90.0 91.0 92.0 93.0 94.0 95.0 96.0 97.0 98.0 99.0 100.0

Polypeptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
1	55	116462	KIDNNOT01	116462H1 (KIDNNOT01), 116462R1 (KIDNNOT01), 116462X304D1 (KIDNNOT01), 1500439F6 (SINTBST01), 2369977F6 (ADRENOT07)
2	56	1210462	BRSTNOT02	260707H1 (HNT2RAT01), 1210462H1 (BRSTNOT02), 1458882F6 (COLNFET02), 1841248T6 (COLNNOT07), 2378362H1 (ISUTNOT01), 3728643F6 (SMCCNN03)
3	57	1305252	PLACNOT02	794067R6 (OVARNOT03), 871909F1 (LUNGAST01), 1235253F1 (LUNGAST03), 1305252F6 (PLACNOT02), 1305252H1 (PLACNOT02), 1702358T6.comp (DOONNOT2), 2678307H1.comp (OVARSTUT07), 3221088H1.comp (COLNNON03), 3647280H1 (ENDINOT01)
4	58	1416289	BRAINOT12	639958R6 (BRSTNOT03), 861752H1 (BRAITUT03), 1416289H1 (BRAINOT12), 1416289X310B1 (BRAINOT12), 1416289X310D2 (BRAINOT12), 1947451R6 (PITUNOT01)
5	59	1558289	SPLNNOT04	1258289H1 (SPLNNOT04), 1852450T6 (LUNGFEOT03), 2396092F6 (THPLAZT01), 2593326T7F6 (LUNGNOT22), 2632784F6 (COLNUTUT2)
6	60	1577739	LINDNOT03	181265R1 (PLACNOB01), 1577739H1 (LINDNOT03), 4180022T6 (STAIRUT03), 4597046H1 (COLSTUT01), 4860616H1 (PROSTUT09), 4991290H1 (LIVRUT11), 5059810H1 (CONDUT02)
7	61	1752768	LIVRUT01	256106R1 (HNT2RAT01), 258814H1 (HNT2RAT01), 3312247F1 (COLNFET02), 1344279T6 (PROSNOT11), 1350089H1 (LAPRUT02), 1440718F6 (THYRNOT03), 1752768F6 (LIVRUT01), 1752768H1 (LIVRUT01), 1752768T6 (LIVRUT01), 2079106F6 (ISUTNOT01), 289A0612U1
8	62	1887228	BLADUT07	800294F1 (SYNORAB01), 140055F1 (TLYNNOR01), 285207X42 (BOGISTHET02), 516882R6 (MMLR1D701), 1217892T1 (NEUTGMT01), 1887228H1 (BLADUT07), 4323029H1 (TLYMUT01)
9	63	1988468	LUNGAST01	072147R6 (THPLPEB01), 496297H1 (HNT2RAT01), 1362109F6 (LUNGNOT2), 1726095F6 (PROSNOT14), 1726095T6 (PROSNOT14), 1988468H1 (LUNGAST01), 1988468T6 (LUNGAST01), 2232471F6 (PROSNOT16)
10	64	2049176	LIVRFEOT2	2049176H1 (LIVRFEOT2), 2049176T6 (LIVRFEOT2), 2049176X321D1 (LIVRFEOT2)
11	65	2686765	LUNGNOT23	1502858F6 (BRAITUT07), 1956694X315D1 (CONNNOT01), 2022628X307D1 (CONNNOT01), 2686765F6 (LUNGNOT23), 2686765H1 (LUNGNOT23), 2864555H1 (KIDNNOT20), 2887609F6 (SINJNOT02), 3381980H1 (ESOGNOT04)
12	66	3215187	TESTNOT07	131135R6 (FIBRAGT01), 3215187R6 (TESTNOT07), 3215187H1 (TESTNOT07)
13	67	3500375	PROSTUT13	860585R1 (BRAITUT03), 1318501F1 (BLAUNOT04), 1419126F1 (KIDNNOT09), 1483246F6 (CORENOT2), 2238114T6 (FANCTUT02), 327329H1 (PROSNOT01), 3209746F7 (BLADNOT08), 3403213H1 (ESOGNOT03), 41766119H1 (BRAINOT22), 4514606H1 (BRADTUT01)

Table 1 (cont.)

Polypeptide SEQ. ID NO.	Nucleotide SEQ. ID NO.	Clone ID	Library	Fragments
14	68	5080410	LNODNOT11	1270372X300D1 (BRAINO09), 3460603H1 (293TF1T01), 5080410H1 (LUNGNOT11),
15	69	5218248	BRSTNOT35	1808748X15C1 (PROSTUT12), 1808748X16C1 (PROSTUT12),
16	70	0583336	MUSCNOT01	3391894H1 (LUNGNOT28)
17	71	1511488	LUNGNOT14	0583336H1 (MUSCNOT01), 0583336F6 (MUSCNOT01), g2206766, g2069225
18	72	1638819	UTRSNOT06	1436265F1 (PANCNOT08), 1511488H1 (LUNGNOT14), 1511488T6 (LUNGNOT14), 1850020F6 (LUNGNOT03)
19	73	1655123	PROSTUT08	1282638T1 (COLLN0T16), 1638819F6 (UTRSNOT06), 1638819H1 (UTRSNOT06), 3597071H1 (FIBPNOT01), SBRA031813D1, SBRA04133D1, SBRA03785D1
20	74	2553926	THYMN0T03	1271351F1 (TESTTUT02), 135234F1 (LATRTUT02), 1655123H1 (PROSTUT08), 2132188G6 (OVARNOT03), 326525H1 (PLXINT01), 3354010H1 (PROSNOT28), 3741838F6 (MENTNOT1), 3741838T6 (MENTNOT1), SXAF03528V1
21	75	2800717	PENCNOT01	403261F1 (TMLR3DT01), 1869739F6 (SKINBIT01), 2137242T6 (SPLNFE02), 2553926H1 (THYMN0T03), 2553956T6 (THYMN0T03), 3935528H1 (PROSTUT09), 5263918F6 (CONDUT02)
22	76	5664154	BRAUNOT01	411179F1 (BRSTNOT01), 415284R1 (BRSTNOT01), 1458971F1 (COLNFE02), 1600810H1 (BLADNOT03), 1622005F6 (BRAITUT13), 217076F6 (ENDCNOT03), 2520087F6 (BRAITUT21), 2800717H1 (PENCNOT01), 5184583H1 (LUNGNOT03), 5435834H1 (SPLNNOT17), 5872662H1 (COLDIT04)
23	77	017900	HUVELPB01	181534F1 (PACN0B01), SCHAO0262V1
24	78	035102	HUVENOB01	017900H1 (HUYELPB01), 092858F1 (HYPONOB01), 1355543F1 (LATRTUT02), 1353543F6 (LATRTUT02), 1428464F1 (SINTBST01), g1616429
25	79	259983	HNT2RAT01	035102H1 (HUVENOB01), 077722R1 (SYNORAB01), 995133H1 (KIDNTUT01), 1356968T6 (LUNGNOT09), 1963135R6 (BRSTNOT04), 2659921F6 (LUNGNOT09), 3110603H1 (BRSTNOT17)
26	80	926810	BRAINOT04	259131R1 (HNT2RAT01), 259983H1 (HNT2RAT01), 268205R1 (HNT2RAT01), 1305728F1 (PACN0T02)
27	81	1398816	BRAITUT08	926810H1 (BRAINOT04), 3490378T6 (EPGNOT01), 4774848H1 (BRAONOT01), SBIA01080D1, SBIA04006D1, SBIA02273D1, SBIA01121D1
				056398F1 (FIBRN0T01), 1252138F2 (LUNGFE03), 1294556T1 (PGANNOT03), 1398816H1 (BRAITUT08), 1545328R1 (PROSTUT04)

Table 1 (cont.)

Poly peptide SEQ. ID NO.	Nucleotide SEQ. ID NO.	Clone ID	Library	Segments
28	82	1496820	PROSN001	996673H1 (KIDNUT01), 1496820H1 (PROSN001), 2368484F6 (ADREN007), 3071781X303D1 (UTRSN001), 3071781X307B1 (UTRSN001), 3071781X316B2 (UTRSN001), 3071781X316D3 (UTRSN001)
29	83	1514559	PANCTUT01	155766H1 (THPIPL02), 1229952H1 (BRAITUT01), 1337018X11 (COLNUT13), 1360361H1 (LUNGNOT12), 1365811H1 (SCORNO02), 1514559F6 (PANCTUT01), 1514559H1 (PANCTUT01)
30	84	1620092	BRAITUT13	1620092F6 (BRAITUT13), 1620092H1 (BRAITUT13), 1832842H1 (BRAINO01), 1843815R6 (COLNUT08), 1843815T6 (COLNUT08)
31	85	1678765	STOMFET01	1678765F6 (STOMFET01), 1678765H1 (STOMFET01), 2640786H1 (LUNGUT08), 3542276F6 (TONSN003), 4180591H1 (SINTUT03), 4183383H1 (LIVDIR01), 4349212H1 (TLYMTX01), 4718559H1 (BRAIHC02), 5023762H1 (OVARNO03), 5332272H1 (KIDNUT34), 91665766
32	86	1708229	PROSN016	388493R1 (THYMN002), 1503519F1 (BRAITUT07), 1708229H1 (PROSN016), 1725267F6 (PROSN014), 3089258F6 (HERAGN03)
33	87	1806454	SINTNOT13	406723H1 (BOSIHE02), 821556R1 (KERANOT02), 1649621F6 (PROSTU09), 1710552H1 (PROSN016), 1806454F6 (SINTNOT13), 1806454H1 (SINTNOT13), 2526283H1 (BRAITUT21), 3869969H1 (BARNOT03)
34	88	1806850	SINTNOT13	270548H1 (HMTZNOT01), 443885R1 (MPHGN003), 1257235F1 (MENITUT03), 1337438H1 (COLNUT13), 1351820F1 (LATRTUT02), 1544066R1 (PROSTU04), 1806850F6 (SINTNOT13), 1806850H1 (SINTNOT13), 1984108T6 (LUNGAST01), 2921419H1 (SININOT04), 3109392H1 (BRSTUT15)
35	89	1851534	LUNGFT03	1851534H1 (LUNGFT03), 2407345R6 (BSTMNO02), 2757389R6 (THPIAS08), 5513454H1 (BRADDI01), 5629312H1 (ELACPER01)
36	90	1868749	SKINBIT01	1322048F1 (BLADNOT04), 1398330F1 (BRAITUT08), 1437866F6 (PANCTUT08), 1868749F6 (SKINBIT01), 1868749H1 (SKINBIT01), 2279968R6 (PROSN001), 2684670H1 (LUNGNOT23), 4632232H1 (GBLADIT02), 4951533H2 (ENDVUNT01), 5077673H1 (LNDNOT11), 5388496H1 (BRAINO19)
37	91	1980010	LUNGUT03	127747R1 (TESTNOT1), 357561F1 (PROSN001), 357561R1 (PROSN001), 918017R1 (BRSTUT04), 1428117F6 (SINTEST01), 1625808F6 (COLNUT01), 1720753H1 (BLADNOT06), 1912038F6 (COLNUT16), 1980010H1 (LUNGUT03), 3112417F6 (BRSTNOT17), 4174704H1 (SINTNOT21), 4238802H1 (SYNNDIT01), 5499543H1 (BRADDI01), 94537459

Table 1 (cont.)

Polypeptide SEQ. ID NO:	Nucleotide SEQ. ID NO:	Clone ID	Library	Fragments	
38	92	2259032	OVARTUT01	475134H1 (NMLR2DT01), 784284R1 (PROSN0T05), 1264124H1 (SYNORAT05), 1418710F1 (KIDNNOT09), 1697570T6 (BLADTUT05), 1874051F6 (LEUKNOT02), 2187960T6 (PROSN0T26), 2259032H1 (OVARTUT01), 2259032R6 (OVARTUT01), 3406237H1 (ESOGTUT03), 3441729H1 (PENCN0T06), 3555764H1 (LUNGNOT31), 3728010H1 (SMCCN0T3), 3813639H1 (TONSN0T3), 4031501H1 (BRAINOT23), 4274704H1 (PROSTTUT01), 4602450H1 (BRSTN0T07), 43327183 (LUNGNOT05), 2555305F7 (THYMN0T03), 2654667T6 (THYMN0T04), SCHA00290V1, SCHA00266V1, g1748241	
39	93	2359526	LUNGFET05	1667182F6 (BARNOT03), 2359526H1 (LUNGFET05), 2359526X311D1 (LUNGFET05), 2555305F7 (THYMN0T03), 2654667T6 (THYMN0T04), SCHA00290V1, SCHA00266V1, g1748241	
40	94	2456494	ENDANOT01	1860223F6 (PROSN0T18), 2456494H1 (ENDANOT01), 2564671H1 (ADRETUT01), 3618339H1 (EPIPNOT01)	
41	95	2668536	ESOGTUT02	1513847H1 (PANCN0T01), 1669943F6 (BARNOT03), 1669943T6 (BARNOT03), 1721443F6 (BLADNOT06), 2668536H1 (ESOGTUT02), 3438287H1 (PENCN0T05), SBFA00330F1, SCBA05255V1, SCBA01530V1	
42	96	2683225	SINIUCT01	196443R6 (KIDNNOT02), 1243440R6 (LUNGNOT03), 1604540F6 (LUNGNOT15), 2072837H1 (ISUTN0T01), 2683225F6 (SINIUCT01), 2683225H1 (SINIUCT01), 3647874H1 (ENDINOT01), 4029178H1 (BRAINOT23)	
43	97	2797839	NPOLNOT01	460779T6 (KERANOT01), 782663H1 (MYONNOT01), 896898R1 (BRSTN0T05), 1218533H1 (NEUTGN0T01), 1312923F6 (BLADTUT02), 2473746F6 (THP1NOT03), 2481564H1 (SMCANOT01), 2797839H1 (NPOLNOT01), 3350118H1 (BRAITUT24), 4184264H1 (BRABDIR01), 4401265H1 (TESTUT03), 4727770H1 (GBLADIT01), 5080203H1 (LUNGNOT11), 5524886H1 (LIVDIR01)	
44	98	2959521	ADRENOT09	046596H1 (CORNNOT01), 087727R6 (LIVRN0T01), 138475H1 (LIVRN0T01), 167505H1 (LIVRN0T01), 647975H1 (CARCXTAT02), 781084T1 (MYONNOT01), 972191R6 (MUSCN0T2), 1309196H1 (COLNFET02), 2641117H1 (LUNGNOT08), 2913953H1 (KIDNUT15), 2959521H1 (ADRENOT09), 2984654H1 (CARGDIT01), 2985141H1 (CARGDIT01), 3138371H1 (SMCCN0T02), 3386016H1 (ESOGN0T04), 3496187H1 (ADRETUT07), 3614426H1 (EPIPNOT01), 4287819H1 (LIVDIR01), 5395566H1 (LIVRUT13), g505101	
45	99	3082014	BRAUNOT01	182588H1 (PLACN0B01), 645276R6 (BRSTTUT02), 1497811F1 (SINRST01), 2051505F6 (LIVRRET02), 3082014H1 (BRAUNOT01), 3464112F6 (293TE20F1), 4603079H1 (BRSTN0T07)	
46	100	3520701	LUNGNON03	971201H1 (MUSCN0T02), 1544657R6 (PROSTTUT04), 1545570H1 (PROSTTUT04), 1671030F6 (BARNOT03), 1671030T6 (BARNOT03), 2605263F6 (LUNGUTUT07), 3520701H1 (LUNGNON03), 3520701R6 (LUNGNON03)	

Table 1 (cont.)

Polyptide SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
47	101	4184320	BRADDIT02	2156956F6 (BRAINT09), 4184253F6 (BRADIR01), 4184253T6 (BRADIR01), 4184250H1 (BRADDIT02), 4252542F6 (BRADIR01), 47624233H1 (PLACNOT05), 5634642H1 (PLACFER01), G1148809
48	102	4764233	PLACNOT05	47624233H1 (PLACNOT05), 5634642H1 (PLACFER01), G1148809
49	103	4817352	HELATX03	426993R6 (BLADNOT01), 426993T6 (BLADNOT1), 488301R6 (HNT2AGT01), 3779640H1 (BRSTNOT27), 4817352H1 (HELATX03)
50	104	5040573	COLHTUT01	1724126F6 (PROSN014), 1859337F6 (PROSN018), 2026289R6 (KERANOT2), 2026289T6 (KERANOT2), 2122846T6 (BRSTNOT07), 3225302H1 (ADRETUT07), 322214H1 (PTHYN03), 4587178H1 (BRAQNOT01), 4601227H1 (BRSTNOT07), 4885408H1 (LUNLWT01), 5040573H1 (COLHTUT01)
51	105	5627029	PLACFER01	967986R1 (BRSTNOT05), 1534642T6 (SPANOT04), 1700904F6 (BLADTUT05), 1846971R6 (COLMN0T09), 2112727R6 (BRADTUT03), 2112727T6 (BRADTUT03), 2205225F6 (SPINET02), 2828475H1 (TLYMN0T03), 3439165F6 (PENCNOT06), 3604622H1 (LUNGNOT10)
52	106	5678487	293TF2T01	1258787F6 (MENTUT03), 1522008F1 (BLADTUT04), 1597992F6 (BLADNOT03), 2057679H1 (BEPINOT01), 2411504H1 (BSTMN02), 2467956H1 (THYRN0T08), 2739089F6 (OVARNOT09), 2739089T6 (OVARNOT09), 2740762H1 (BRSTTUT14), 2754616H1 (THP1AZS08), 3254971R6 (OVARTUN01), 3487616H1 (EPIGNOT01), 5678487H1 (293TF2T01)
53	107	5682976	BRAENOT02	350492H1 (LVENNOT01), 825361R1 (PROSN0T06), 879866R1 (THRN0T02), 1667502F6 (BRAENOT03), 1713321F6 (BRSTTUT08), 1876248T6 (LEURN0T02), 1962215T6 (BRSTN0T04), 2539188H1 (BONRUT01), 2896448H1 (KIDNUT14), 3141553H1 (SMCCNOT02), 3374826F6 (CONNTUT05), 3773427H1 (BRSTN0T25), 3779981H1 (BRSTN0T27), 5682976H1 (BRAENOT02), 5546853H1 (TESTNOC01)
54	108	5992432	FTUBTUT02	645878R6 (BRSTTUT02), 1287660F1 (BRAINT01), 1287660T6 (BRAINT01), 1417373F6 (BRAINT02), 1618868F6 (BRAINT02), 2269980R6 (UTRN0T02), 2793117F6 (COLNUT16), 3246793F6 (BRAINT01), 3592787H1 (293TF5T01), 5992432H1 (FTUBTUT02), 9821012

Table 2

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
1	145	T10 S93	N15 N38	Signal peptide: M1-Q33 Protein SH3 domain repeat: L8-R99 GLGF signal transduction-related domain: M1-R99		MOTIFS SPSCAN BLAST_PRODOM BLAST_DOMO
2	340	T39 S190 S268 T307 S88 S102 S165 S226 S230 S234 T337		P120 nuclear proliferating cell antigen: N117-K333 Proliferative cell nuclear protein P120: E26-G293	Proliferating cell nuclear antigen p120 (g2649749) A. fulgidus	MOTIFS BLAST_PRODOM BLAST_DOMO BLAST_GenBank
3	418	S246 S415 T142 T156 S292 S349 S369 S64 S247 S298	N190 N191 N203 N288 N306		Candidate tumor suppressor p33ING1 (g2829208) H. sapiens	MOTIFS BLAST_GenBank
4	297	T217 T82 S76 S127 S176 T207 S246 Y189	N74	Germ cell-less protein: E96-N297	Germ cell-less suppressor protein (g5814404) Mus musculus	MOTIFS BLINPS_PFAM BLAST_GenBank
5	184	T34 S103 S5 T136	N76		Differentiation factor MDC-3.13 (g3860093) H. sapiens	MOTIFS BLAST_GenBank
6	173	S109 S24 S59 S66 S141 S142 T152			Posterior end mark-5 (g4107015) C. savignyi	MOTIFS BLAST_GenBank

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
7	591	S582 T71 T208 S217 S339 T475 S493 T536 S45 S105 S153 T208 S305 S336 T578 Y93	N374 N425 N534 N585	Signal peptide M1-L64 TPR domain mitosis control E239-P356 TPR repeat V265-K516	Cell division cycle protein 23 homolog (g5541721) <u>A. thaliana</u>	MOTIFS SPSCAN HMMR_PFBM BLAST_DOMO BLAST_GenBank
8	463	T237 S34 T67 T117 T125 S138 T288 T321 S328 S418 T80 S186 S190 S209 S210 T232 T288 S418 T441 S445 Y416	N208	Formin limb deformity: M1-E335	Lymphocyte specific formin related protein (g4101720) <u>M. musculus</u>	MOTIFS BLAST_PRODOM BLAST_DOMO BLAST_GenBank
9	270		N64 N94 N147		Early embryogenesis MRG1 protein (g2570051) <u>M. musculus</u>	MOTIFS BLAST_GenBank
10	255	S180 T49 T53 S97 S152 T201 S210 S23 S97 T145 T216 S225 S228 T231 S242 Y106 Y240		Polyposis locus TB2 homolog: G15-T117 Polyposis locus protein: V13-T117	Similar to polyposis locus protein 1 (g849238) <u>H. sapiens</u>	MOTIFS BLAST_PRODOM BLAST_DOMO BLAST_GenBank
11	533	S227 S412 S505 S7 S17 S65 T349 S442 T29 S72 S89 S358 S442 T446 S505 Y244		TRE oncogene: R56-1277	TRE oncogene-related protein (g2286196) <u>D. melanogaster</u>	MOTIFS BLOCKS_DOMO BLAST_GenBank

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
12	160	S40		Signal peptide: M1-A30 Transmembrane domain: A6-129 Cornichon developmental Protein: M1-S160	Cornichon-like protein (g4521254) <u>M. musculus</u>	MOTIFS SPSCAN HMMR BLAST_PRODOM BLAST_DOMO BLAST_GenBank
13	531	S195 T196 S357 T45 S172 T199 S212 S322 S465 T495 T45 T241 S255 T279 T319 S328 S3 T67 S104	N244 N401		Cdc 73p (g632679) <u>S. cerevisiae</u>	MOTIFS BLAST_GenBank
14	165				Wolf-Hirschhorn syndrome candidate 2 protein (g3860187) <u>H. sapiens</u>	MOTIFS BLAST_GenBank
15	199	S2 S21 S69 T102 S189			Developmental protein DG118 (g3789911) <u>D. discoideum</u>	MOTIFS BLAST_GenBank
16	168	S141 S55 S61 T79	N77	Signal peptide M1-S61 H-Rev protein homolog P15-K166	G377529 retinoic acid receptor responder 3 <u>Homo sapiens</u>	BLAST_GenBank SPSCAN BLAST_PRODOM MOTIFS
17	162	S70 S85 T16 T28 T65 T80 T100 S127 Y111			G207250 growth and transformation dependent protein <u>Rattus norvegicus</u>	BLAST_GenBank

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
18	246	T209 S227 T243 T28 S223 S51 S136 S201	N26 N158	Protein cell intergenic region FTSJ K25-K241	g2529303 cell division protein J Methanobacterium thermoautotrophicum gl322234	BLAST-GenBank BLAST-PRODOM BLAST-DOMO MOTIFS
19	483	T394 T65 S86 S219 S225 T230 S298 T239 T472 S114 S200 T273 S371 T407 T424 T431		Signal peptide M1-G29 OS-9 precursor L54-E281	BLAST-GenBank SPSCAN BLAST-PRODOM MOTIFS	
20	280	T129 T6 T102 T119 T181 S250 S46 T72 T84 S262		Signal peptide M1-L28	g3901272 ZW10 interactor Zwint Homo sapiens	BLAST-GenBank SPSCAN MOTIFS
21	425	S122 S235 T60 S192 S203 S204 S218 S226 S307 T313 S332 S366 S370 T375 T402 S409 S89 S118 S241 S284 T360 Y399	N190 N311		g455719 Activated c-raf oncogenic fusion protein homolog Homo sapiens	BLAST-GenBank
22	128	S3 S107	N42	Prenyl group binding site (CAAX box) C125-P128 Ovarian granulosa cell 13.0 KD protein HGR74 N16-P128	g4580592 brain expressed X-linked protein 2 Mus musculus	BLAST-GenBank MOTIFS BLAST-PRODOM
23	113	S88 T20 T37		Biotin-requiring enzyme attachment site: L40-L90	LDOC-1 protein g3869127 (Homo sapiens) Nagasaki, K. et al. (1999) Cancer Lett. 140:227-234.	BLAST-GenBank PROFILESAN MOTIFS

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
24	308	S95 T79 T98 S184 S246 S251 T55 S184 S226 S294 S300 Y127	N77	Melanoma antigen gene (MAGE) family: M1-Q200, H205-D283, D91-A287	Breast cancer associated gene 1 94928044 (Homo sapiens) Lurquin, C. et al. (1997) Genomics 46:397-408.	BLAST-GenBank BLAST-PRODOM HMMER-PFAM BLAST-DBOM MOTIFS
25	221	S145 S160 S217 S25 S31 S70 S85 T89 S153 S197 Y34	N139	Annexin VI signature: L86-V95 Sushi domain: T165-C174	Teratocarcinoma expressed gene Tera g1575505 (Mus musculus)	BLAST-GenBank BLINPS-PRINTS BLINPS-PFAM MOTIFS
26	402	T344 S39 S78 S109 S237 T269 S273 T376 T381 T383 S11 S49 T89 T344 S364 S11	N76 N107 N171 N362		Paraneoplastic cancer-testis-brain antigen g6179740 (Homo sapiens)	BLAST-GenBank MOTIFS
27	93				Hypoxia inducible gene-1 g4929330 (Homo sapiens)	BLAST-GenBank MOTIFS
28	353	S125 T42 S43 S85 S212 S283 S114 T42 S49 S105 S120 S133 S162 S163 S212 S290	N145 N157 N191	af-4 (FEL protein): S195-K353 E4-Q185	AF5q31 protein g6601438 (Homo sapiens)	BLAST-GenBank BLAST-PRODOM BLAST-DBOM MOTIFS
29	120	T57		Cyclin-dependent kinase inhibitor: D7-P106, M1-N114	Cyclin dependent kinase inhibitor CIP1 g2276312 (Homo sapiens)	BLAST-GenBank BLAST-PRODOM BLAST-DBOM MOTIFS

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
30	144	S15 S64		Transmembrane domain: 193-1110	Transformation dependent protein g207250 (Rattus norvegicus) N.Glaichenhaus and P.Cuzin (1987) Cell 50:1081-1089.	BLAST-GenBank MOTIFS HMMER
31	933	S603 T51 S109 T129 S162 S203 S223 S224 S240 S261 S266 S280 S282 S313 T328 S346 S353 S378 S394 S460 S491 S499 T531 S627 S641 S642 S725 T732 S759 S188 S309 S423 S592 S671 S675 T706 S771 Y856	N107 N238 N639 N883		Replication protein Smp2 g218488 (Saccharomyces cerevisiae) Irie, K. et al. (1993) Mol. Gen. Genet. 6:283-288.	BLAST-GenBank MOTIFS
32	268	S7 T104 T154 S169	N90	Serine-Threonine Kinase Binder MP81: L74-I230	Putative mitotic protein (Schizosaccharomyces pombe) g3947877 F.C.Luca and M.Winey (1998) Mol Biol Cell 9:29-46.	BLAST-GenBank BLAST-PRODOM MOTIFS

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
33	337	T29 S236 T44 T238		Leucine zipper: L259-L280, L266-L287	DNA binding protein g184390 (Homo sapiens) Weitzel, J.N. et al. (1992) Genomics 14:309- 319.	BLAST-GenBank MOTIFS
34	565	T17 S34 S61 S66 T138 T142 S174 T238 S245 S265 S436 S466 S527 S106 S205 S218 S258 T297 S314 T325 S463 T470 Y460	N347 N386 N506	F-Box domain: H75-Y123, L82-N95 Disease resistance protein: G254-I270	P-box protein FLR1 g7672734 (Homo sapiens)	BLAST-GenBank HMMER_PFBM BLIMPS-PRINTS MOTIFS
35	228	S200 T47 T62 S78 S107 S188 S192 S206 S200 S205 S213	N36 N94 N225		Predicted WHSCL protein (Wolf- Hirschhorn syndrome critical region 1) g4378022 (Homo sapiens) Stecic I. et al. (1998) Hum. Mol. Genet. 7:1071- 1082.	BLAST-GenBank MOTIFS
36	495	S451 S152 S365 S478 S108 S171 S181 T192 T347 T409 S435 Y86 Y111 Y203			Malignant brain tumor protein 1(3)mbt g3811111 (Homo sapiens) Koga, H. et al. (1999) Oncogene 18:3799-3809.	BLAST-GenBank MOTIFS

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
37	1336	T635 T769 S902 S10 S32 S33 T76 S95 S156 T298 S313 T427 S467 T579 T626 T642 S661 T668 S680 T699 T729 S774 S834 T859 T915 S944 S959 S961 S997 S1049 T1085 S1132 S1227 T1245 S1249 T48 S94 T169 S224 T352 T379 T389 T475 T696 S867 T883 T889 S940 S961 S1220 Y631	N148 N152 N345 N385 N1213 N1247	Ribosomal protein S14 signature: R1172-N1194 Leucine zipper: L211-L232	Neuroblastoma related protein g4337460 (Homo sapiens)	BLAST-GenBank BLIMPS-PRINTS MOTIFS
38	934	T532 S11 T23 T80 S171 S202 T214 T240 S244 T275 S412 S416 S437 S518 T523 S719 S746 S753 S796 S807 S93 T279 T527 S598 T780	N8 N210 N426	SAP: I92-Q364	Sap2 family putative cell cycle dependent phosphatase g3426127 (Schizosaccharomyc es pombe) Luke, M.M. et al. (1996) Mol. Cell Biol. 16:2744-2755.	BLAST-GenBank BLAST-DMO MOTIFS

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
39	515	T72 S122 S175 S272 S277 S305 T420 S422 T432 T79 S139 T189 S215 T316 S457 T486 Y13 Y383	N16 N31 N115	Metastasis-Associated Protein: E65-R230 Leucine zipper: L234-L255	Metastasis associated gene g1008544 (Homo sapiens) Toh, Y. et al. (1995) Gene 159:97-104 Toh, Y. et al. (1994) J Biol. Chem. 269:22958-22963.	BLAST-GenBank BLAST-PRODOM BLIMPS-PRINTS MOTIFS
40	146	S51		Leucine zipper: L5-L26, L12-L33, L19-L40 Cyclin: H19-K262	LDQC1 g3869127 (Homo sapiens) Cyclin K g3746549 (Homo sapiens) Edwards, M.C. et al. (1998) Mol. Cell Biol. 18:4291-4300.	BLAST-GenBank BLIMPS-PFAM MOTIFS BLAST-GenBank BLAST-PRODOM MOTIFS
41	580	S324 S36 S340 S550 S86 T109 T119 T150 T226 S329 S340	N190			
42	131	S78 T121 T26		Presenilin: Q64-K75	Cell growth regulator DRR1 g4322559 (Homo sapiens) G. Thomas and M.N.Hall (1997) Curr. Opin. Cell Biol. 9:782-787.	BLAST-GenBank BLIMPS-PRINTS MOTIFS

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
43	812	S44 S588 S646 S801 S111 S120 S134 T140 S148 S150 S181 T185 S262 S279 S440 T477 S497 T520 T542 T605 S675 S40 T64 T311 T316 T319 T505 S562 S565 T566 T695 S702 S707 S708 T739 T776 S790 Y277	N503 N618	NOL1/NOR2/fmu(sun) family signature: F454-G467, F300-K585, T388-W402, G410-G433, F454-G467, K507-L532, E189-W576 Proliferating Cell Nucleolar Antigen P120: M1-S134, E135- T311, F587-G805	Proliferating cell nuclear protein P120 g287723 (Homo sapiens)	BLAST-GenBank BLAST-PRODOM BLAST-DMO BLIMPS-BLOCKS MOTIFS HMMER-PFAM
44	537	S505 T69 S138 S194 S310 S337 S356 T386 S485 S37 T45 T282	N122 N132 N147	Transmembrane domains: 1506-G532, V271-L290, W472-F490	Estrogen induced protein in breast cancer LIV-1 g1256001 (Homo sapiens)	BLAST-GenBank HMMER MOTIFS
45	584	S185 T324 S343 T537 S575 S17 T102 S128 T229 T374 S412 T450	N28	Cytochrome C motif: C283-T288 Metastasis- associated protein MTA1: R19-R143, D144-K321, G340-G483, P432-K555 Leucine zipper: L147-L168	Metastasis associated gene g1008544 (Homo sapiens) Toh, Y. et al. (1995) Gene 159:97-104 Toh, Y. et al. (1994) J. Biol. Chem. 269:22958-22963..	BLAST-GenBank BLAST-PRODOM MOTIFS

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
46	425	S190 T301 S12 S19 S41 S205 T206 T235 S263 S265 T315 S43 S52 S85 T93 T351 S411 Y422	N275	MLO2 mitosis-associated protein: L24-R188, P226-Y245, N308-E408		BLAST-PRODOM MOTIFS
47	255	T9 T147 S237	N144	Melastatin: M1-R172, G199-G255	Melastatin g3047242 (Mus musculus) Duncan, L.M. et al. (1998) Cancer Res. 58:1515-1520.	BLAST-GenBank BLAST-PRODOM MOTIFS
48	111	T30 S2 T8			Melanoma associated antigen GAGE-8 g3511023 (Homo sapiens) Van den Eynde, B. et al. (1995) J. Exp. Med. 182:689-698.	BLAST-GenBank MOTIFS
49	422	T110 T159 S136 S150 T163 T190 S383 T413 S9 T27 S46 S96 T347 S359 S363 S368 Y350		XPMC2 (mitosis associated inducing protein): A236-E402	Mitotic regulator XPMC2 (Xenopus gene which prevents mitotic catastrophe) g595380 (Xenopus laevis) J.-Y. Su and J.-L. Maller (1995) Mol. Gen. Genet. 246:387-396.	BLAST-GenBank BLAST-PRODOM BLAST-DBO MOTIFS

Table 2 (cont.)

Polypeptide SEQ ID NO:	Amino Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
50	397	S20 S21 T395 T57 S59 T64 S127 S208 T210 S262 S307 T341 T64 T168 S180 S185 S218 S231 S288 S326	N222 N260	Transmembrane motifs: I361-L380, L24-L44 Cell division control protein: K17-L347	Cell cycle protein CDC1 g550426 (Saccharomyces cerevisiae)	BLAST-GenBank HMMER BLAST-PRODOM MOTIFS
51	800	S56 S448 T721 S760 S48 S84 S111 S119 T146 T189 T235 S250 S265 T275 S321 S335 T392 S448 T466 S474 T562 S596 S598 T626 S686 S3 S4 S65 S89 S107 T123 S348 T398 T402 T716 S730 S738 T743 S789 Y102 Y216 Y569 Y685	N554 N665	Signal peptide: M1-A25 Leucine zipper: L365-L386	SART-1 g4126469 (Mus musculus)	BLAST-GenBank SPSCAN MOTIFS
52	713	S200 T631 S8 T9 S20 T42 T114 T121 T172 T177 T191 T192 S218 T231 T256 S325 S335 S381 T464 T482 T538 T581 T617 S693 S94 S166 T201 S202 S321 T568 S614 T658 Y459	N7 N49 N462	Leucine zipper: L680-L701	Colon cancer antigen NY-CO-8 g3170180 (Homo sapiens) Scanlan, M.J. et al. (1998) Int. J. Cancer 76:652-658.	BLAST-GenBank BLAST-PRODOM BLAST-DMO MOTIFS

Polypeptide SQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs and Domains	Homologous Sequences	Analytical Methods and Databases
53	880	S18 S68 T123 T143 S159 T178 T282 S294 S327 T736 S388 T397 T403 S426 S438 S474 S563 T587 T634 T645 S659 S665 S677 S756 S799 S809 T827 S870 S82 T88 S99 T131 T165 S215 S253 S362 S487 T510 S525 S589 T593 S622	N60 N251 N338 N514 N585 N643	Myb1 DNA-binding domain: W808-I816 WD40 domains: L41-N79, K84-N124, T131-D170, G239-D281, A771-S809, F157-T171 Acidic Serine Cluster Repeat: A423-R697	homologous to mouse gene PC326 g458632 (Homo sapiens) Bergsagel, P.L. et al. (1992) Oncogene 7:2059-2064.	BLAST-GenBank BLAST-DBO HMMER-PFAM BLIPS-PRINTS MOTIFS
54	855	T460 S8 S179 S261 T288 T313 T377 T706 T761 T755 S764 S803 S851 S34 S67 T129 S190 S339 T391 S483 S502 S537 Y92	N552	Crooked neck protein (RNA processing associated, contains TPR repeat): W398-V814	Predicted TPR domain protein G2315362 (Caenorhabditis elegans) Zhang, K. et al. (1991) Genes Dev. 5:1080-1091.	BLAST-GenBank BLAST-PRODOM MOTIFS

Table 3

Nucleotide SEQ ID NO:	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition Fraction of Total	Vector
55	263-307	Cardiovascular (0.200) Gastrointestinal (0.200) Reproductive (0.222)	Cancer (0.433) Inflammation (0.267) Cell Proliferation (0.200)	PBLUESCRIPT
56	406-450	Reproductive (0.222) Cardiovascular (0.167) Gastrointestinal (0.167) Nervous (0.167)	Cancer (0.500) Inflammation (0.389) Cell Proliferation (0.167)	PSPORT1
57	1001-1045	Reproductive (0.265) Gastrointestinal (0.206) Nervous	Cancer (0.412) Inflammation (0.324) Cell Proliferation (0.176)	pINCY
58	226-270	Nervous (0.316) Hematopoietic/Immune (0.211) Reproductive (0.211)	Cancer (0.368) Inflammation (0.368) Cell Proliferation (0.158)	pINCY
59	406-450	Hematopoietic/Immune (0.500) Cardiovascular (0.227)	Cancer (0.182) Inflammation (0.682) Cell Proliferation (0.136)	pINCY
60	56-100	Gastrointestinal (0.545) Nervous (0.182)	Cancer (0.545) Inflammation (0.364) Cell Proliferation (0.273)	pINCY
61	1046-1090	Reproductive (0.182) Nervous (0.271) Reproductive (0.220)	Cancer (0.542) Inflammation (0.288) Cell Proliferation (0.220)	pINCY
62	226-270	Gastrointestinal (0.153) Hematopoietic/Immune (0.288) Nervous (0.178)	Cancer (0.397) Inflammation (0.548)	pINCY
63	559-603	Reproductive (0.164) Reproductive (0.260) Gastrointestinal (0.145) Cardiovascular (0.130)	Cancer (0.458) Inflammation (0.359) Cell Proliferation (0.176)	PSPORT1
64	12-56	Reproductive (0.385) Gastrointestinal (0.231) Cardiovascular (0.154) Nervous (0.154)	Cancer (0.538) Inflammation (0.154) Cell Proliferation (0.154)	pINCY
65	488-532 1091-1135	Reproductive (0.308) Nervous (0.282) Gastrointestinal (0.154)	Cancer (0.487) Inflammation (0.231) Cell Proliferation (0.103)	pINCY

Table 3 (cont.)

Nucleotide Seq ID NO:	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition Fraction of Total	Vector
66	37-81	Nervous (0.500) Dermatologic (0.250) Reproductive (0.250)	Inflammation (0.500)	pINCY
67	326-370 1136-1180	Nervous (0.237) Reproductive (0.237) Hematopoietic/Immune (0.158)	Cancer (0.395) Inflammation (0.316) Cell Proliferation (0.158)	pINCY
68	451-495	Nervous (0.312) Reproductive (0.312) Developmental (0.125) Hematopoietic/Immune (0.125) Urologic (0.125)	Cancer (0.562) Inflammation (0.188) Cell Proliferation (0.312)	pINCY
69	64-108	Reproductive (0.233) Nervous (0.174) Cardiovascular (0.140)	Cancer (0.477) Inflammation (0.279) Cell Proliferation (0.198)	pINCY
70	77-121	Cardiovascular (0.500) Musculoskeletal (0.500)	Cancer (0.500) Trauma (0.500)	PBLUESCRIPT
71	164-208	Developmental (0.222) Nervous (0.222)	Cancer (0.444) Cell proliferation (0.222) Trauma (0.222)	pINCY
72	604-648	Reproductive (0.362) Gastrointestinal (0.149) Hematopoietic/Immune (0.128)	Cancer (0.426) Inflammation/Trauma (0.276) Cell proliferation (0.170)	pINCY
73	106-150 1066-1110	Reproductive (0.307) Nervous (0.202) Cardiovascular (0.114)	Cancer (0.482) Inflammation/Trauma (0.307) Cell proliferation (0.175)	pINCY
74	651-695	Hematopoietic/Immune (0.290) Reproductive (0.226) Cardiovascular (0.161)	Inflammation/Trauma (0.451) Cell proliferation (0.230) Cancer (0.320)	pINCY
75	241-285 535-579	Reproductive (0.193) Cardiovascular (0.169) Gastrointestinal (0.157)	Cancer (0.458) Inflammation/Trauma (0.337) Cell proliferation (0.169)	pINCY

Table 3 (cont.)

Nucleotide Seq ID NO:	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition Fraction of Total	Vector
76	173-217 593-637	Nervous (0.513) Reproductive (0.167)	Inflammation/Trauma (0.371) Cancer (0.333) Cell proliferation (0.141)	pINCY
77	13-57	Reproductive (0.241) Nervous (0.202) Cardiovascular (0.140)	Cancer (0.461) Inflammation (0.180) Cell Proliferation (0.167)	PBLUESCRIPT
78	176-220	Nervous (0.279) Reproductive (0.235) Gastrointestinal (0.147)	Cancer (0.500) Inflammation (0.176) Cell Proliferation (0.162)	PBLUESCRIPT
79	79-123	Nervous (0.280) Cardiovascular (0.160) Developmental (0.160)	Cancer (0.480) Cell Proliferation (0.480) Inflammation (0.160)	PBLUESCRIPT
80	870-914	Nervous (0.571) Reproductive (0.238) Developmental (0.095)	Cancer (0.238) Inflammation (0.381) Cell Proliferation (0.190)	PSPORT1
81	149-194	Nervous (0.216) Reproductive (0.201) Gastrointestinal (0.185)	Cancer (0.432) Inflammation (0.259) Cell Proliferation (0.154)	pINCY
82	150-194	Reproductive (0.375) Cardiovascular (0.125) Endocrine (0.125) Hematopoietic/Immune (0.125) Developmental (0.125) Urologic (0.125)	Cancer (0.375) Inflammation (0.375) Trauma (0.250)	PSPORT1
83	177-221	Reproductive (0.199) Gastrointestinal (0.173) Hematopoietic/Immune (0.128) Nervous (0.128)	Cancer (0.429) Inflammation (0.270) Cell Proliferation (0.186)	pINCY
84	342-386	Reproductive (0.252) Gastrointestinal (0.196) Nervous (0.161)	Cancer (0.483) Inflammation (0.238) Cell Proliferation (0.161)	pINCY
85	124-168	Hematopoietic/Immune (0.308) Cardiovascular (0.154) Nervous (0.154) Gastrointestinal (0.154)	Cancer (0.538) Inflammation (0.308)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition Fraction of Total	Vector
86	238-282	Reproductive (0.277) Cardiovascular (0.181) Nervous (0.169)	Cancer (0.434) Inflammation (0.193) Cell Proliferation (0.157)	pINCY
87	117-161	Reproductive (0.250) Gastrointestinal (0.250) Hematopoietic/Immune (0.115)	Cancer (0.558) Inflammation (0.192) Cell Proliferation (0.115) Trauma (0.115)	pINCY
88	139-183	Nervous (0.237) Reproductive (0.214) Gastrointestinal (0.168)	Cancer (0.397) Inflammation (0.298) Trauma (0.137)	pINCY
89	184-228 352-396	Reproductive (0.556) Nervous (0.222) Hematopoietic/Immune (0.111) Developmental (0.111)	Cancer (0.444) Inflammation (0.333) Cell Proliferation (0.333)	pINCY
90	69-113 879-923	Nervous (0.316) Reproductive (0.193) Hematopoietic/Immune (0.158)	Cancer (0.439) Inflammation (0.211) Cell Proliferation (0.123)	pINCY
91	72-116	Nervous (0.211) Reproductive (0.197) Gastrointestinal (0.158)	Cancer (0.461) Inflammation (0.263) Cell Proliferation (0.211)	PSPORT1
92	489-533	Reproductive (0.274) Nervous (0.217) Gastrointestinal (0.123)	Cancer (0.481) Inflammation (0.189) Cell Proliferation (0.160)	PSPORT1
93	761-805	Reproductive (0.219) Hematopoietic/Immune (0.156) Developmental (0.125)	Cancer (0.312) Cell Proliferation (0.281) Inflammation (0.188) Trauma (0.188)	PSPORT1
94	126-170	Reproductive (0.379) Nervous (0.241) Developmental (0.138)	Cancer (0.414) Cell Proliferation (0.241) Inflammation (0.103)	PBLUESCRIPT
95	1173-1217	Reproductive (0.192) Gastrointestinal (0.192) Nervous (0.173)	Cancer (0.481) Inflammation (0.250) Cell Proliferation (0.212)	pINCY
96	465-509	Hematopoietic/Immune (0.250) Cardiovascular (0.158) Gastrointestinal (0.145)	Inflammation (0.368) Cancer (0.355) Cell Proliferation (0.132)	pINCY

Table 3 (cont.)

Nucleotide SEQ ID NO:	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition Fraction of Total	Vector
97	2427-2471	Nervous (0.224) Reproductive (0.197) Gastrointestinal (0.184)	Cancer (0.474) Cell Proliferation (0.263) Inflammation (0.237)	pINCY
98	23-67	Gastrointestinal (0.270) Reproductive (0.190) Cardiovascular (0.135)	Cancer (0.429) Inflammation (0.278) Cell Proliferation (0.143)	pINCY
99	106-150	Gastrointestinal (0.263) Reproductive (0.263) Nervous (0.158)	Cancer (0.474) Inflammation (0.368) Cell Proliferation (0.211)	pINCY
100	73-117 460-504	Hematopoietic/Immune (0.211) Reproductive (0.211) Cardiovascular (0.105) Developmental (0.105) Gastrointestinal (0.105) Musculoskeletal (0.105)	Cancer (0.474) Inflammation (0.263) Cell Proliferation (0.211)	PSPORT1
101	861-905	Developmental (0.333) Nervous (0.667)	Cell Proliferation (0.333) Trauma (0.333) Neurological (0.333)	pINCY
102	8-52	Developmental (1.000)	Cell Proliferation (1.000)	pINCY
103	199-243	Hematopoietic/Immune (0.143) Nervous (0.179) Reproductive (0.286)	Cancer (0.536) Inflammation (0.250) Cell Proliferation (0.214)	pINCY
104	413-457 908-952	Nervous (0.236) Reproductive (0.222) Gastrointestinal (0.125)	Cancer (0.458) Inflammation (0.236) Cell Proliferation (0.139)	pINCY
105		Reproductive (0.270) Gastrointestinal (0.169) Hematopoietic/Immune (0.101) Developmental (0.101)	Cancer (0.449) Inflammation (0.281) Cell Proliferation (0.258)	pINCY
106	255-299 513-557	Reproductive (0.216) Gastrointestinal (0.196) Nervous (0.157)	Cancer (0.490) Inflammation (0.176) Cell Proliferation (0.176)	pINCY
107	167-211 814-859 1922-1966	Reproductive (0.263) Nervous (0.162) Gastrointestinal (0.141)	Cancer (0.455) Inflammation (0.202) Trauma (0.131)	pINCY

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Table 3 (cont.)

Nucleotide SEQ ID NO:	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition Fraction of Total	Vector
108	877-921 2230-2274	Reproductive (0.299) Nervous (0.206) Gastrointestinal (0.134)	Cancer (0.536) Inflammation (0.227) Cell Proliferation(0.124)	pINCY

Table 4

Nucleotide SEQ ID NO:	Library	Library Description
55	KIDNNOT01	Library was constructed using RNA isolated from the kidney tissue of a 64-year-old Caucasian female, who died from an intracranial bleed. Patient history included rheumatoid arthritis.
56	BRSTNOT02	Library was constructed using RNA isolated from diseased breast tissue removed from a 55-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated proliferative fibrocystic changes characterized by apocrine metaplasia, sclerosing adenosis, cyst formation, and ductal hyperplasia without atypia. Pathology for the associated tumor tissue indicated an invasive grade 4 mammary adenocarcinoma. Patient history included atrial tachycardia and a benign neoplasm. Family history included cardiovascular and cerebrovascular disease.
57	PLACNOT02	Library was constructed using RNA isolated from the placental tissue of a Hispanic female fetus, who was prematurely delivered at 21 weeks' gestation. Serologies of the mother's blood were positive for CMV (cytomegalovirus).
58	BRAINOT12	Library was constructed using RNA isolated from brain tissue removed from the right frontal lobe of a 5-year-old Caucasian male during a hemispherectomy. Pathology indicated extensive polymicrogyria and mild to moderate gliosis (predominantly subpial and subcortical), which are consistent with chronic seizure disorder. Family history included a cervical neoplasm.
59	SPLNNOT04	Library was constructed using RNA isolated from the spleen tissue of a 2-year-old Hispanic male, who died from cerebral anoxia.
60	LUNGNOT03	Library was constructed using RNA isolated from lymph node tissue obtained from a 67-year-old Caucasian male during a segmental lung resection and bronchoscopy. On microscopic exam, this tissue was found to be extensively necrotic with 10% viable tumor. Pathology for the associated tumor tissue indicated invasive grade 3-4 squamous cell carcinoma. Patient history included hemangioma. Family history included atherosclerotic coronary artery disease, benign hypertension, congestive heart failure, atherosclerotic coronary artery disease.
61	LIVRTUT01	Library was constructed using RNA isolated from liver tumor tissue removed from a 51-year-old Caucasian female during a hepatic lobectomy. Pathology indicated metastatic grade 3 adenocarcinoma consistent with colon cancer. Family history included a malignant neoplasm of the liver.

Table 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Description
62	BLADTUT07	Library was constructed using RNA isolated from bladder tumor tissue removed from the anterior bladder wall of a 58-year-old Caucasian male during a radical cystectomy, radical prostatectomy, and gastrectomy. Pathology indicated a grade 3 transitional cell carcinoma in the left lateral bladder. Patient history included angina, emphysema, and tobacco use. Family history included acute myocardial infarction, atherosclerotic coronary artery disease, and type II diabetes.
63	LUNGAST01	Library was constructed using RNA isolated from the lung tissue of a 17-year-old Caucasian male, who died from head trauma. Patient history included asthma.
64	LIVREFET02	Library was constructed using RNA isolated from liver tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation.
65	LUNGNOT23	Library was constructed using RNA isolated from left lobe lung tissue removed from a 58-year-old Caucasian male. Pathology for the associated tumor tissue indicated metastatic grade 3 (of 4) osteosarcoma. Patient history included soft tissue cancer, secondary cancer of the lung, prostate cancer, and an acute duodenal ulcer with hemorrhage. Family history included prostate cancer, breast cancer, and acute leukemia.
66	TESTNOT07	Library was constructed using RNA isolated from testicular tissue removed from a 31-year-old Caucasian male during an unilateral orchiectomy (excision of testis). Pathology indicated a mass containing a large subcapsular hematoma with laceration of the tunica albuginea. The surrounding testicular parenchyma was extensively necrotic.
67	PROSTUT13	Library was constructed using RNA isolated from prostate tumor tissue removed from a 59-year-old Caucasian male during a radical prostatectomy with regional lymph node excision. Pathology indicated adenocarcinoma (Gleason grade 3+3). Adenofibromatous hyperplasia was present. The patient presented with elevated prostate-specific antigen (PSA). Patient history included colon diverticuli, asbestosis, and thrombophlebitis. Family history included multiple myeloma, hyperlipidemia, and rheumatoid arthritis.
68	LNODNOT11	Library was constructed using RNA isolated from lymph node tissue removed from a 16-month-old Caucasian male who died from head trauma. Patient history included bronchitis.

Table 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Description
69	BRSTNOT35	Library was constructed using RNA isolated from breast tissue removed from a 46-year-old Caucasian female during a bilateral reduction mastopasty. Pathology indicated normal breast parenchyma, bilaterally. The patient presented with hypertrophy of breast and headache. Patient history included obesity, lumbago, glaucoma, and alcohol abuse. Family history included cataract, osteoarthritis, uterine cancer, benign hypertension, hyperlipidemia, alcohol cirrhosis of the liver, cerebrovascular disease, and type II diabetes.
70	MUSCNOT01	Library was constructed at Stratagene (STR937209), using RNA isolated from the skeletal muscle tissue of a patient with malignant hyperthermia.
71	LUNGNOT14	Library was constructed using RNA isolated from lung tissue removed from the left lower lobe of a 47-year-old Caucasian male during a segmental lung resection. Pathology for the associated tumor tissue indicated a grade 4 adenocarcinoma, and the parenchyma showed calcified granuloma. Patient history included benign hypertension and chronic obstructive pulmonary disease. Family history included type II diabetes and acute myocardial infarction.
72	UTRSNOT06	Library was constructed using RNA isolated from myometrial tissue removed from a 50-year-old Caucasian female during a vaginal hysterectomy. Pathology indicated residual atypical complex endometrial hyperplasia. Pathology for the associated tissue removed during dilation and curettage indicated fragments of atypical complex hyperplasia and a single microscopic focus suspicious for grade 1 adenocarcinoma. Patient history included benign breast neoplasm, hypothyroid disease, polypectomy, and arthralgia. Family history included cerebrovascular disease, atherosclerotic coronary artery disease, hyperlipidemia, and chronic hepatitis.
73	PROSTUT08	Library was constructed using RNA isolated from prostate tumor tissue removed from a 60-year-old Caucasian male during radical prostatectomy and regional lymph node excision. Pathology indicated an adenocarcinoma (Gleason grade 3+4). Adenofibromatous hyperplasia was also present. The patient presented with elevated prostate specific antigen (PSA). Patient history included a kidney cyst, and hematuria. Family history included tuberculosis, cerebrovascular disease, and atherosclerotic coronary artery disease.
74	THYMNOT03	Library was constructed using RNA isolated from thymus tissue removed from a 21-year-old Caucasian male during a thymectomy. Pathology indicated an unremarkable thymus and a benign parathyroid adenoma in the right inferior parathyroid. Patient history included atopic dermatitis, a benign neoplasm of the parathyroid, and tobacco use. Family history included atherosclerotic coronary artery disease and benign hypertension.

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Table 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Description
75	PENCNOT01	Library was constructed using RNA isolated from penis corpus cavernosum tissue removed from a 53-year-old male. Patient history included untreated penile carcinoma.
76	BRAUNOT01	Library was constructed using RNA isolated from caudate/putamen/nucleus accumbens tissue removed from the brain of a 35-year-old Caucasian male who died from cardiac failure. Pathology indicated moderate leptomeningeal fibrosis and multiple microinfarctions of the cerebral neocortex. Patient history included dilated cardiomyopathy, congestive heart failure, cardiomegaly and an enlarged spleen and liver.
77	HUVELP801	This library was constructed using RNA isolated from HUV-EC-C (ATCC CRL 1730) cells stimulated with cytokine/LPS. RNA was isolated from two pools of HUV-EC-C cells that had been treated with either 4 units/ml TNF-alpha and 2 units/ml gamma IFN for 96 hours, or 1 unit/ml IL-1 beta and 100 ng/ml LPS for 5 hours.
78	HUVENB01	This library was constructed using RNA isolated from HUV-EC-C (ATCC CRL 1730) cells.
79	HNT2BAT01	This library was constructed at Stratagene (STR937231), using RNA isolated from the hNT2 cell line (derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor). Cells were treated with retinoic acid for 24 hours.
80	BRAINOT04	This library was constructed using RNA isolated from the brain tissue of a 44-year-old Caucasian male with a cerebral hemorrhage. The tissue, which contained coagulated blood, came from the choroid plexus of the right anterior temporal lobe. Family history included coronary artery disease and myocardial infarction.
81	BRAITUT08	This library was constructed using RNA isolated from brain tumor tissue removed from the left frontal lobe of a 47-year-old Caucasian male during excision of cerebral meningeal tissue. Pathology indicated grade 4 fibrillary astrocytoma with focal tumoral radionecrosis. Patient history included cerebrovascular disease, deficiency anemia, hyperlipidemia and epilepsy. Family history included cerebrovascular disease and a malignant prostate neoplasm.
82	PROSNON01	This library was constructed from 4.4 million independent clones from a prostate library. Starting RNA was made from prostate tissue removed from a 28-year-old Caucasian male who died from a self-inflicted gunshot wound. The normalization and hybridization conditions were adapted from Soares, M.B. et al. (1994) Proc. Natl. Acad. Sci. USA 91:9228-9232, using a longer (19 hour) reannealing hybridization period.

Table 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Description
83	PANCTUT01	This library was constructed using RNA isolated from pancreatic tumor tissue removed from a 65-year-old Caucasian female during radical subtotal pancreatectomy. Pathology indicated an invasive grade 2 adenocarcinoma. Patient history included type II diabetes, osteoarthritis, cardiovascular disease, benign neoplasm in the large bowel, and a cataract. Previous surgeries included a total splenectomy, cholecystectomy, and abdominal hysterectomy. Family history included cardiovascular disease, type II diabetes, and stomach cancer.
84	BRAITUT13	This library was constructed using RNA isolated from brain tumor tissue removed from the left frontal lobe of a 68-year-old Caucasian male during excision of a cerebral meningeal lesion. Pathology indicated a meningioma in the left frontal lobe.
85	STOMFET01	This library was constructed using RNA isolated from the stomach tissue of a Caucasian female fetus, who died at 20 weeks' gestation.
86	PROSNOT16	This library was constructed using RNA isolated from diseased prostate tissue removed from a 68-year-old Caucasian male during a radical prostatectomy. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma (Gleason grade 3+4). The patient presented with elevated prostate specific antigen (PSA). During this hospitalization, the patient was diagnosed with myasthenia gravis. Patient history included osteoarthritis and type II diabetes. Family history included benign hypertension, acute myocardial infarction, hyperlipidemia, and arteriosclerotic coronary artery disease.
87	SINTNOT13	This library was constructed using RNA isolated from ileum tissue obtained from a 25-year-old Asian female during a partial colectomy and temporary ileostomy. Pathology indicated moderately active chronic ulcerative colitis, involving colonic mucosa from the distal margin to the ascending colon. Family history included hyperlipidemia, depressive disorder, malignant cervical neoplasm, viral hepatitis A, and depressive disorder.
88	SINTNOT13	This library was constructed using RNA isolated from ileum tissue obtained from a 25-year-old Asian female during a partial colectomy and temporary ileostomy. Pathology indicated moderately active chronic ulcerative colitis, involving colonic mucosa from the distal margin to the ascending colon. Family history included hyperlipidemia, depressive disorder, malignant cervical neoplasm, viral hepatitis A, and depressive disorder.
89	LUNGFET03	This library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation.
90	SKINBIT01	This library was constructed using RNA isolated from diseased skin tissue of the left lower leg. Patient history included erythema nodosum of the left lower leg.

Table 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Description
91	LUNGUT03	This library was constructed using RNA isolated from lung tumor tissue removed from the left lower lobe of a 69-year-old Caucasian male during segmental lung resection. Pathology indicated residual grade 3 invasive squamous cell carcinoma. Patient history included acute myocardial infarction, prostatic hyperplasia, malignant skin neoplasm, and tobacco use.
92	OVARTUT01	This library was constructed using RNA isolated from ovarian tumor tissue removed from a 43-year-old Caucasian female during removal of the fallopian tubes and ovaries. Pathology indicated grade 2 mucinous cystadenocarcinoma involving the entire left ovary. Patient history included mitral valve disorder, pneumonia, and viral hepatitis. Family history included atherosclerotic coronary artery disease, pancreatic cancer, stress reaction, cerebrovascular disease, breast cancer, and uterine cancer.
93	LUNGFET05	This library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation from anencephalus.
94	ENDANOT01	This library was constructed using RNA isolated from aortic endothelial cell tissue from an explanted heart removed from a male during a heart transplant.
95	ESOGTUT02	This library was constructed using RNA isolated from esophageal tumor tissue obtained from a 61-year-old Caucasian male during a partial esophagectomy, proximal gastrectomy, pyloromyotomy, and regional lymph node excision. Pathology indicated an invasive grade 3 adenocarcinoma in the esophagus. Family history included atherosclerotic coronary artery disease, type II diabetes, chronic liver disease, primary cardiomyopathy, benign hypertension, and cerebrovascular disease.
96	SINIUCT01	This library was constructed using RNA isolated from ileum tissue obtained from a 42-year-old Caucasian male during a total intra-abdominal colectomy and endoscopic jejunostomy. Previous surgeries included polypectomy, colonoscopy, and spinal canal exploration. Family history included cerebrovascular disease, benign hypertension, atherosclerotic coronary artery disease, and type II diabetes.
97	NPOLNOT01	This library was constructed using RNA isolated from nasal polyp tissue removed from a 78-year-old Caucasian male during a nasal polypectomy. Pathology indicated a nasal polyp and striking eosinophilia. Patient history included asthma and nasal polyps.
98	ADRENUT09	This library was constructed using RNA isolated from left adrenal gland tissue removed from a 43-year-old Caucasian male during nephroureterectomy, regional lymph node excision, and unilateral left adrenalectomy. Pathology for the associated tumor tissue indicated a grade 2 renal cell carcinoma mass in the posterior lower pole of the left kidney with invasion into the renal pelvis.

Table 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Description
99	BRAJUNT01	This library was constructed using RNA isolated from SK-N-MC, a neuroepithelioma cell line (ATCC HTB-10) derived from a 14-year-old Caucasian female with neuroepithelioma, with metastasis to the supra-orbital area.
100	LUNGNON03	This library was constructed from 2.56 x 1e6 independent clones from a lung tissue library. RNA was made from lung tissue removed from the left lobe a 58-year-old Caucasian male during a segmental lung resection. Pathology for the associated tumor tissue indicated a metastatic grade 3 (of 4) osteosarcoma. Patient history included soft tissue cancer, secondary cancer of the lung, prostate cancer, and an acute duodenal ulcer with hemorrhage. Patient also received radiation therapy to the retroperitoneum. Family history included prostate cancer, breast cancer, and acute leukemia. The normalization and hybridization conditions were adapted from Soares et al., PNAS (1994) 91:9228; Swarcop et al., NAR (1991) 19:1954; and Bonaldo et al., Genome Research (1996) 6:791.
101	BRADDIT02	This library was constructed using RNA isolated from diseased choroid plexus tissue of the lateral ventricle removed from the brain of a 57-year-old Caucasian male, who died from a cerebrovascular accident. Patient history included Huntington's disease, and emphysema.
102	PLACNOT05	This library was constructed using RNA isolated from placental tissue removed from a Caucasian male fetus, who died after 18 weeks' gestation from fetal demise.
103	HELATYT03	This library was constructed using RNA isolated from a treated Hela cell line, derived from cervical adenocarcinoma removed from a 31-year-old Black female. The cells were treated with 1 microM PMA and 100 microM cycloheximide for 24 hours.
104	COLHUT01	This library was constructed using RNA isolated from colon tumor tissue removed from the hepatic flexure of a 55-year-old Caucasian male during right hemicolectomy, incidental appendectomy, and permanent colostomy. Pathology indicated invasive grade 3 adenocarcinoma. Patient history included benign hypertension, anxiety, abnormal blood chemistry, blepharitis, heart block, osteoporosis, acne, and hyperplasia of prostate. Family history included prostate cancer, acute myocardial infarction, stroke, and atherosclerotic coronary artery disease.
105	PLACFER01	This library was constructed using RNA isolated from placental tissue removed from a Caucasian fetus who died after 16 weeks' gestation from fetal demise and hydrocephalus. Serology was positive for CMV antibody.
106	293T2T01	This library was constructed using RNA isolated from a treated, transformed embryonal cell line (293-EBNA) derived from kidney epithelial tissue. The cells were treated with 5-aza-2'-deoxycytidine and transformed with adenovirus 5 DNA.

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Table 5

Program	Description	Reference	Parameter Threshold
ABI FACTURA	A program that removes vector sequences and masks ambiguous bases in nucleic acid sequences.	PE Biosystems, Foster City, CA.	
ABUPARACEL FDF	A Fast Data Finder useful in comparing and annotating amino acid or nucleic acid sequences.	PE Biosystems, Foster City, CA; Paracel Inc., Pasadena, CA.	Mismatch <50%
ABI AutoAssembler	A program that assembles nucleic acid sequences.	PE Biosystems, Foster City, CA.	
BLAST	A Basic Local Alignment Search Tool useful in sequence similarity search for amino acid and nucleic acid sequences. BLAST includes five functions: blastp, blastn, blastx, tblastn, and tblastx.	Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410; Altschul, S.F. et al. (1997) Nucleic Acids Res. 25:3389-3402.	ESTs: Probability value= 1.0E-8 or less Full Length sequences: Probability value= 1.0E-10 or less
FASTA	A Pearson and Lipman algorithm that searches for similarity between a query sequence and a group of sequences of the same type. FASTA comprises at least five functions: fasta, ifasta, fastx, ifastx, and search.	Pearson, W.R. and D.J. Lipman (1988) Proc. Natl. Acad. Sci. USA 85:2444-2448; Pearson, W.R. (1990) Methods Enzymol. 183:63-98; and Smith, T.F. and M.S. Waterman (1981) Adv. Appl. Math. 2:482-489.	ESTs: fasta E value=1.0E-6 Assembled ESTs: fasta Identity= 95% or greater and Match length=200 bases or greater; fasta E value=1.0E-8 or less Full Length sequences: fasta score=100 or greater
BLIMPS	A BLocks IMProved Searcher that matches a sequence against those in BLOCKS, PRINTS, DOMO, PRODOM, and PFAM databases to search for gene families, sequence homology, and structural fingerprint regions.	Henikoff, S. and J.G. Henikoff (1991) Nucleic Acids Res. 19:6565-6572; Henikoff, J.G. and S. Henikoff (1996) Methods Enzymol. 266:88-105; and Altmood, T.K. et al. (1997) J. Chem. Inf. Comput. Sci. 37:417-424.	Score=1000 or greater; Ratio of Score/Strength = 0.75 or larger; and, if applicable, Probability value= 1.0E-3 or less
HIMMER	An algorithm for searching a query sequence against hidden Markov model (HMM)-based databases of protein family consensus sequences, such as PFAM.	Krogh, A. et al. (1994) J. Mol. Biol. 235:1501-1531; Somnhammer, E.L.L. et al. (1988) Nucleic Acids Res. 26:320-322.	Score=10-50 bits for PFAM hits, depending on individual protein families

Table 5 (cont.)

Program	Description	Reference	Parameter Threshold
ProfileScan	An algorithm that searches for structural and sequence motifs in protein sequences that match sequence patterns defined in Prosite.	Gribkov, M. et al. (1988) CABIOS 4:61-66; Gribkov, M. et al. (1989) Methods Enzymol. 183:146-159; Bairoch, A. et al. (1997) Nucleic Acids Res. 25:217-221.	Normalized quality score > GCG-specified "HIGH" value for that particular Prosite motif. Generally, scores=1-4.2.1.
Phred	A base-calling algorithm that examines automated sequencer traces with high sensitivity and probability.	Ewing, B. et al. (1998) Genome Res. 8:175-185; Ewing, B. and P. Green (1998) Genome Res. 8:186-194.	
Phrap	A Phils Revised Assembly Program including SWAT and CrossMatch, programs based on efficient implementation of the Smith-Waterman algorithm, useful in searching sequence homology and assembling DNA sequences.	Smith, T.F. and M.S. Waterman (1981) Adv. Appl. Math. 2:482-489; Smith, T.F. and M.S. Waterman (1981) J. Mol. Biol. 147:195-197; and Green, P., University of Washington, Seattle, WA.	Scores= 120 or greater; Match length= 56 or greater
Consed	A graphical tool for viewing and editing Phrap assemblies.	Gordon, D. et al. (1998) Genome Res. 8:195-202.	
SPScan	A weight matrix analysis program that scans protein sequences for the presence of secretory signal peptides.	Nielson, H. et al. (1997) Protein Engineering 10:1-6; Claverie, J.M. and S. Audic (1997) CABIOS 12:431-439.	Scores=3.5 or greater
Motifs	A program that searches amino acid sequences for patterns that matched those defined in Prosite.	Bairoch, A. et al. (1997) Nucleic Acids Res. 25:217-221; Wisconsin Package Program Manual, version 9, page M51-59, Genetics Computer Group, Madison, WI.	

What is claimed is:

1. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:
 - 5 a) an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32,
 - 10 SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ ID NO:54,
 - b) a naturally occurring amino acid sequence having at least 90% sequence identity to an
 - 15 amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33,
 - 20 SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ ID NO:54,
 - c) a biologically active fragment of an amino acid sequence selected from the group
 - 25 consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID
 - 30 NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ ID NO:54, and
 - d) an immunogenic fragment of an amino acid sequence selected from the group consisting
 - 35 of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID

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NO:15, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ ID NO:54.

2. An isolated polypeptide of claim 1 selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ ID NO:54.

3. An isolated polynucleotide encoding a polypeptide of claim 1.

20 4. An isolated polynucleotide encoding a polypeptide of claim 2.

5. An isolated polynucleotide of claim 4 selected from the group consisting of SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, and SEQ ID NO:108.

6. A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 3.

35 7. A cell transformed with a recombinant polynucleotide of claim 6.

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8. A transgenic organism comprising a recombinant polynucleotide of claim 6.

9. A method for producing a polypeptide of claim 1, the method comprising:

- a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 1, and
- b) recovering the polypeptide so expressed.

10. 10. An isolated antibody which specifically binds to a polypeptide of claim 1.

11. An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:

- a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, and SEQ ID NO:108,
- b) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, and SEQ ID NO:108,
- c) a polynucleotide sequence complementary to a),
- d) a polynucleotide sequence complementary to b), and
- e) an RNA equivalent of a)-d).

12. An isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of claim 11.

13. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

- a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and
- b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

14. A method of claim 13, wherein the probe comprises at least 60 contiguous nucleotides.

15. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

- a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and
- b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

16. A composition comprising an effective amount of a polypeptide of claim 1 and a pharmaceutically acceptable excipient.

17. A composition of claim 16, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ ID NO:54.

18. A method for treating a disease or condition associated with decreased expression of

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functional CCYPR, comprising administering to a patient in need of such treatment the composition of claim 16.

19. A method for screening a compound for effectiveness as an agonist of a polypeptide of claim 1, the method comprising:

- a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
- b) detecting agonist activity in the sample.

20. A composition comprising an agonist compound identified by a method of claim 19 and a pharmaceutically acceptable excipient.

21. A method for treating a disease or condition associated with decreased expression of functional CCYPR, comprising administering to a patient in need of such treatment a composition of claim 20.

15

22. A method for screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, the method comprising:

- a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
- b) detecting antagonist activity in the sample.

20

23. A composition comprising an antagonist compound identified by a method of claim 22 and a pharmaceutically acceptable excipient.

24. A method for treating a disease or condition associated with overexpression of functional CCYPR, comprising administering to a patient in need of such treatment a composition of claim 23.

25

25. A method of screening for a compound that specifically binds to the polypeptide of claim 1, said method comprising the steps of:

30

- a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and
- b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.

26. A method of screening for a compound that modulates the activity of the polypeptide of claim 1, said method comprising:

35

a) combining the polypeptide of claim 1 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 1,

b) assessing the activity of the polypeptide of claim 1 in the presence of the test compound, and

- 5 c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.

- 10 27. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

- a) exposing a sample comprising the target polynucleotide to a compound, and
b) detecting altered expression of the target polynucleotide.

15

28. A method for assessing toxicity of a test compound, said method comprising:

- a) treating a biological sample containing nucleic acids with the test compound;
b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific
20 hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 11 or fragment thereof;
c) quantifying the amount of hybridization complex; and
d) comparing the amount of hybridization complex in the treated biological sample with the
25 amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

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SEQUENCE LISTING

<110> INCYTE GENOMICS, INC.
 HILLMAN, Jennifer L.
 LAL, Preeti
 TANG, Y. Tom
 YUE, Henry
 AU-YOUNG, Janice
 BANDMAN, Olga
 AZIMZAI, Yalda
 YANG, Junming
 LU, Dyung Aina M.
 BAUGHN, Mariah R.
 PATTERSON, Chandra
 SHAH, Purvi

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Gln Pro Leu Ile Asn Val Ile Lys Val Ser Glu Leu Asp Gly Arg
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Lys Glu Asn Thr Leu Gly Cys Arg Asn Asn Asn Ser Thr Ala Ser
185    190    195
Ser Asn Asn Ala Tyr Asn Val Asn Ser Ser Gln Pro Leu Gly Ser
200    205    210
Tyr Asn Ile Gly Ser Leu Ser Ser Gly Thr Gly Ala Gly Ala Ile
215    220    225
Thr Met Ala Ala Ala Gln Ala Val Gln Ala Thr Ala Gln Met Lys
230    235    240
Glu Gly Arg Arg Thr Ser Ser Leu Lys Ala Ser Tyr Glu Ala Phe
245    250    255
Lys Asn Asn Asp Phe Gln Leu Gly Lys Glu Phe Ser Met Ala Arg
260    265    270
Glu Thr Val Gly Tyr Ser Ser Ser Ser Ala Leu Met Thr Thr Leu
275    280    285
Thr Gln Asn Ala Ser Ser Ser Ala Ala Asp Ser Arg Ser Gly Arg
290    295    300
Lys Ser Lys Asn Asn Asn Lys Ser Ser Ser Gln Gln Ser Ser Ser
305    310    315
Ser Ser Ser Ser Ser Ser Leu Ser Ser Cys Ser Ser Ser Ser Thr
320    325    330
Val Val Gln Glu Ile Ser Gln Gln Thr Thr Val Val Pro Glu Ser
335    340    345
Asp Ser Asn Ser Gln Val Asp Trp Thr Tyr Asp Pro Asn Glu Pro
350    355    360
Arg Tyr Cys Ile Cys Asn Gln Val Ser Tyr Gly Glu Met Val Gly
365    370    375
Cys Asp Asn Gln Asp Cys Pro Ile Glu Trp Phe His Tyr Gly Cys
380    385    390
Val Gly Leu Thr Glu Ala Pro Lys Gly Lys Trp Tyr Cys Pro Gln
395    400    405
Cys Thr Ala Ala Met Lys Arg Arg Gly Ser Arg His Lys
410    415

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<210> 4

<211> 297

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

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<223> Incyte ID No: 1416289CD1

<400> 4

Met	Ala	Tyr	Asn	Val	Ile	Ile	Ile	Tyr	Phe	Asn	Phe	Arg	Cys	Leu	15
1				5					10						15
Glu	Trp	Leu	Leu	Asn	Asn	Leu	Met	Thr	His	Gln	Asn	Val	Glu	Leu	30
				20					25						30
Phe	Lys	Glu	Leu	Ser	Ile	Asn	Val	Met	Lys	Gln	Leu	Ile	Gly	Ser	45
				35					40						45
Ser	Asn	Leu	Phe	Val	Met	Gln	Val	Glu	Met	Asp	Ile	Tyr	Thr	Ala	60
				50					55						60
Leu	Lys	Lys	Trp	Met	Phe	Leu	Gln	Leu	Val	Pro	Ser	Trp	Asn	Gly	75
				65					70						75
Ser	Leu	Lys	Gln	Leu	Leu	Thr	Glu	Thr	Asp	Val	Trp	Phe	Ser	Lys	90
				80					85						90
Gln	Arg	Lys	Asp	Phe	Glu	Gly	Met	Ala	Phe	Leu	Glu	Thr	Glu	Gln	105
				95					100						105
Gly	Lys	Pro	Phe	Val	Ser	Val	Phe	Arg	His	Leu	Arg	Leu	Gln	Tyr	120
				110					115						120
Ile	Ile	Ser	Asp	Leu	Ala	Ser	Ala	Arg	Ile	Ile	Glu	Gln	Asp	Ala	135
				125					130						135
Val	Val	Pro	Ser	Glu	Trp	Leu	Ser	Ser	Val	Tyr	Lys	Gln	Gln	Trp	150
				140					145						150
Phe	Ala	Met	Leu	Arg	Ala	Glu	Gln	Asp	Ser	Glu	Val	Gly	Pro	Gln	165
				155					160						165
Glu	Ile	Asn	Lys	Glu	Glu	Leu	Glu	Gly	Asn	Ser	Met	Arg	Cys	Gly	180
				170					175						180
Arg	Lys	Leu	Ala	Lys	Asp	Gly	Glu	Tyr	Cys	Trp	Arg	Trp	Thr	Gly	195
				185					190						195
Phe	Asn	Phe	Gly	Phe	Asp	Leu	Leu	Val	Thr	Tyr	Thr	Asn	Arg	Tyr	210
				200					205						210
Ile	Ile	Phe	Lys	Arg	Asn	Thr	Leu	Asn	Gln	Pro	Cys	Ser	Gly	Ser	225
				215					220						225
Val	Ser	Leu	Gln	Pro	Arg	Arg	Ser	Ile	Ala	Phe	Arg	Leu	Arg	Leu	240
				230					235						240
Ala	Ser	Phe	Asp	Ser	Ser	Gly	Lys	Leu	Ile	Cys	Ser	Arg	Thr	Thr	255
				245					250						255
Gly	Tyr	Gln	Ile	Leu	Thr	Leu	Glu	Lys	Asp	Gln	Glu	Gln	Val	Val	270
				260					265						270
Met	Asn	Leu	Asp	Ser	Arg	Leu	Leu	Ile	Phe	Pro	Leu	Tyr	Ile	Cys	285
				275					280						285
Cys	Asn	Phe	Leu	Tyr	Ile	Ser	Pro	Glu	Lys	Lys	Asn				
				290					295						

<210> 5

<211> 184

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1558289CD1

<400> 5

Met	Glu	Ser	Phe	Ser	Ser	Lys	Ser	Leu	Ala	Leu	Gln	Ala	Glu	Lys	15
1				5					10						15
Lys	Leu	Leu	Ser	Lys	Met	Ala	Gly	Arg	Ser	Val	Ala	His	Leu	Phe	30
				20					25						30
Ile	Asp	Glu	Thr	Ser	Ser	Glu	Val	Leu	Asp	Glu	Leu	Tyr	Arg	Val	45
				35					40						45
Ser	Lys	Glu	Tyr	Thr	His	Ser	Arg	Pro	Gln	Ala	Gln	Arg	Val	Ile	60
				50					55						60
Lys	Asp	Leu	Ile	Lys	Val	Ala	Ile	Lys	Val	Ala	Val	Leu	His	Arg	75
				65					70						75

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Asn	Gly	Ser	Phe	Gly	Pro	Ser	Glu	Leu	Ala	Leu	Ala	Thr	Arg	Phe	
				80					85					90	
Arg	Gln	Lys	Leu	Arg	Gln	Gly	Ala	Met	Thr	Ala	Leu	Ser	Phe	Gly	
				95					100					105	
Glu	Val	Asp	Phe	Thr	Phe	Glu	Ala	Ala	Val	Leu	Ala	Gly	Leu	Leu	
				110					115					120	
Thr	Glu	Cys	Arg	Asp	Val	Leu	Leu	Glu	Leu	Val	Glu	His	His	Leu	
				125					130					135	
Thr	Pro	Lys	Ser	His	Gly	Arg	Ile	Arg	His	Val	Phe	Asp	His	Phe	
				140					145					150	
Ser	Asp	Pro	Gly	Leu	Leu	Thr	Ala	Leu	Tyr	Gly	Pro	Asp	Phe	Thr	
				155					160					165	
Gln	His	Leu	Gly	Lys	Ile	Cys	Asp	Gly	Leu	Arg	Lys	Leu	Leu	Asp	
				170					175					180	
Glu	Gly	Lys	Leu												

<210> 6

<211> 173

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1577739CD1

<400> 6

Met	Asp	Val	Arg	Arg	Val	Leu	Val	Lys	Ala	Glu	Met	Glu	Lys	Phe	
1				5					10					15	
Leu	Gln	Asn	Lys	Glu	Leu	Phe	Ser	Ser	Leu	Lys	Lys	Gly	Lys	Ile	
				20					25					30	
Cys	Cys	Cys	Cys	Arg	Ala	Lys	Phe	Pro	Leu	Phe	Ser	Trp	Pro	Pro	
				35					40					45	
Ser	Cys	Leu	Phe	Cys	Lys	Arg	Ala	Val	Cys	Thr	Ser	Cys	Ser	Ile	
				50					55					60	
Lys	Met	Lys	Met	Pro	Ser	Lys	Lys	Phe	Gly	His	Ile	Pro	Val	Tyr	
				65					70					75	
Thr	Leu	Gly	Phe	Glu	Ser	Pro	Gln	Arg	Val	Ser	Ala	Ala	Lys	Thr	
				80					85					90	
Ala	Pro	Ile	Gln	Arg	Arg	Asp	Ile	Phe	Gln	Ser	Leu	Gln	Gly	Pro	
				95					100					105	
Gln	Trp	Gln	Ser	Val	Glu	Glu	Ala	Phe	Pro	His	Ile	Tyr	Ser	His	
				110					115					120	
Gly	Cys	Val	Leu	Lys	Asp	Val	Cys	Ser	Glu	Cys	Thr	Ser	Phe	Val	
				125					130					135	
Ala	Asp	Val	Val	Arg	Ser	Ser	Arg	Lys	Ser	Val	Asp	Val	Leu	Asn	
				140					145					150	
Thr	Thr	Pro	Arg	Arg	Ser	Arg	Gln	Thr	Gln	Ser	Leu	Tyr	Ile	Pro	
				155					160					165	
Asn	Thr	Arg	Thr	Leu	Asp	Phe	Lys								
				170											

<210> 7

<211> 591

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1752768CD1

<400> 7

Met	Val	Pro	Val	Ala	Val	Thr	Ala	Ala	Val	Ala	Pro	Val	Leu	Ser	
1				5					10					15	
Ile	Asn	Ser	Asp	Phe	Ser	Asp	Leu	Arg	Glu	Ile	Lys	Lys	Gln	Leu	

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20	25	30
Leu Leu Ile Ala Gly Leu Thr Arg Glu	Arg Gly Leu Leu His Ser	
35	40	45
Ser Lys Trp Ser Ala Glu Leu Ala Phe	Ser Leu Pro Ala Leu Pro	
50	55	60
Leu Ala Glu Leu Gln Pro Pro Pro Pro	Ile Thr Glu Glu Asp Ala	
65	70	75
Gln Asp Met Asp Ala Tyr Thr Leu Ala	Lys Ala Tyr Phe Asp Val	
80	85	90
Lys Glu Tyr Asp Arg Ala Ala His Phe	Leu His Gly Cys Asn Ser	
95	100	105
Lys Lys Ala Tyr Phe Leu Tyr Met Tyr	Ser Arg Tyr Leu Ser Gly	
110	115	120
Glu Lys Lys Lys Asp Asp Glu Thr Val	Asp Ser Leu Gly Pro Leu	
125	130	135
Glu Lys Gly Gln Val Lys Asn Glu Ala	Leu Arg Glu Leu Arg Val	
140	145	150
Glu Leu Ser Lys Lys His Gln Ala Arg	Glu Leu Asp Gly Phe Gly	
155	160	165
Leu Tyr Leu Tyr Gly Val Val Leu Arg	Lys Leu Asp Leu Val Lys	
170	175	180
Glu Ala Ile Asp Val Phe Val Glu Ala	Thr His Val Leu Pro Leu	
185	190	195
His Trp Gly Ala Trp Leu Glu Leu Cys	Asn Leu Ile Thr Asp Lys	
200	205	210
Glu Met Leu Lys Phe Leu Ser Leu Pro	Asp Thr Trp Met Lys Glu	
215	220	225
Phe Phe Leu Ala His Ile Tyr Thr Glu	Leu Gln Leu Ile Glu Glu	
230	235	240
Ala Leu Gln Lys Tyr Gln Asn Leu Ile	Asp Val Gly Phe Ser Lys	
245	250	255
Ser Ser Tyr Ile Val Ser Gln Ile Ala	Val Ala Tyr His Asn Ile	
260	265	270
Arg Asp Ile Asp Lys Ala Leu Ser Ile	Phe Asn Glu Leu Arg Lys	
275	280	285
Gln Asp Pro Tyr Arg Ile Glu Asn Met	Asp Thr Phe Ser Asn Leu	
290	295	300
Leu Tyr Val Arg Ser Met Lys Ser Glu	Leu Ser Tyr Leu Ala His	
305	310	315
Asn Leu Cys Glu Ile Asp Lys Tyr Arg	Val Glu Thr Cys Cys Val	
320	325	330
Ile Gly Asn Tyr Tyr Ser Leu Arg Ser	Gln His Glu Lys Ala Ala	
335	340	345
Leu Tyr Phe Gln Arg Ala Leu Lys Leu	Asn Pro Arg Tyr Leu Gly	
350	355	360
Ala Trp Thr Leu Met Gly His Glu Tyr	Met Glu Met Lys Asn Thr	
365	370	375
Ser Ala Ala Ile Gln Ala Tyr Arg His	Ala Ile Glu Val Asn Lys	
380	385	390
Arg Asp Tyr Arg Ala Trp Tyr Gly Leu	Gly Gln Thr Tyr Glu Ile	
395	400	405
Leu Lys Met Pro Phe Tyr Cys Leu Tyr	Tyr Cys Arg Arg Ala His	
410	415	420
Gln Leu Arg Pro Asn Asp Ser Arg Met	Leu Val Ala Leu Gly Glu	
425	430	435
Cys Tyr Glu Lys Leu Asn Gln Leu Val	Glu Ala Lys Lys Cys Tyr	
440	445	450
Trp Arg Ala Tyr Ala Val Gly Asp Val	Glu Lys Met Ala Leu Val	
455	460	465
Lys Leu Ala Lys Leu His Glu Gln Leu	Thr Glu Ser Glu Gln Ala	
470	475	480
Ala Gln Cys Tyr Ile Lys Tyr Ile Gln	Asp Ile Tyr Ser Cys Gly	
485	490	495

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Glu	Ile	Val	Glu	His	Leu	Glu	Glu	Ser	Thr	Ala	Phe	Arg	Tyr	Leu
				500					505					510
Ala	Gln	Tyr	Tyr	Phe	Lys	Cys	Lys	Leu	Trp	Asp	Glu	Ala	Ser	Thr
				515					520					525
Cys	Ala	Gln	Lys	Cys	Cys	Ala	Phe	Asn	Asp	Thr	Arg	Glu	Glu	Gly
				530					535					540
Lys	Ala	Leu	Leu	Arg	Gln	Ile	Leu	Gln	Leu	Arg	Asn	Gln	Gly	Glu
				545					550					555
Thr	Pro	Thr	Thr	Glu	Val	Pro	Ala	Pro	Phe	Phe	Leu	Pro	Ala	Ser
				560					565					570
Leu	Ser	Ala	Asn	Asn	Thr	Pro	Thr	Arg	Arg	Val	Ser	Pro	Leu	Asn
				575					580					585
Leu	Ser	Ser	Val	Thr	Pro									
				590										

<210> 8

<211> 463

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1887228CD1

<400> 8

Met	Pro	Leu	Leu	Asn	Trp	Val	Ala	Leu	Lys	Pro	Ser	Gln	Ile	Thr
1				5					10					15
Gly	Thr	Val	Phe	Thr	Glu	Leu	Asn	Asp	Glu	Lys	Val	Leu	Gln	Glu
				20					25					30
Leu	Asp	Met	Ser	Asp	Phe	Glu	Glu	Gln	Phe	Lys	Thr	Lys	Ser	Gln
				35					40					45
Gly	Pro	Ser	Leu	Asp	Leu	Ser	Ala	Leu	Lys	Ser	Lys	Ala	Ala	Gln
				50					55					60
Lys	Ala	Pro	Ser	Lys	Ala	Thr	Leu	Ile	Glu	Ala	Asn	Arg	Ala	Lys
				65					70					75
Asn	Leu	Ala	Ile	Thr	Leu	Arg	Lys	Gly	Asn	Leu	Gly	Ala	Glu	Arg
				80					85					90
Ile	Cys	Gln	Ala	Ile	Glu	Ala	Tyr	Asp	Leu	Gln	Ala	Leu	Gly	Leu
				95					100					105
Asp	Phe	Leu	Glu	Leu	Leu	Met	Arg	Phe	Leu	Pro	Thr	Glu	Tyr	Glu
				110					115					120
Arg	Ser	Leu	Ile	Thr	Arg	Phe	Glu	Arg	Glu	Gln	Arg	Pro	Met	Glu
				125					130					135
Glu	Leu	Ser	Glu	Glu	Asp	Arg	Phe	Met	Leu	Cys	Phe	Ser	Arg	Ile
				140					145					150
Pro	Arg	Leu	Pro	Glu	Arg	Met	Thr	Thr	Leu	Thr	Phe	Leu	Gly	Asn
				155					160					165
Phe	Pro	Asp	Thr	Ala	Gln	Leu	Leu	Met	Pro	Gln	Leu	Asn	Ala	Ile
				170					175					180
Ile	Ala	Ala	Ser	Met	Ser	Ile	Lys	Ser	Ser	Asp	Lys	Leu	Arg	Gln
				185					190					195
Ile	Leu	Glu	Ile	Val	Leu	Ala	Phe	Gly	Asn	Tyr	Met	Asn	Ser	Ser
				200					205					210
Lys	Arg	Gly	Ala	Ala	Tyr	Gly	Phe	Arg	Leu	Gln	Ser	Leu	Asp	Ala
				215					220					225
Leu	Leu	Glu	Met	Lys	Ser	Thr	Asp	Arg	Lys	Gln	Thr	Leu	Leu	His
				230					235					240
Tyr	Leu	Val	Lys	Val	Ile	Ala	Glu	Lys	Tyr	Pro	Gln	Leu	Thr	Gly
				245					250					255
Phe	His	Ser	Asp	Leu	His	Phe	Leu	Asp	Lys	Ala	Gly	Ser	Val	Ser
				260					265					270
Leu	Asp	Ser	Val	Leu	Ala	Asp	Val	Arg	Ser	Leu	Gln	Arg	Gly	Leu
				275					280					285
Glu	Leu	Thr	Gln	Arg	Glu	Phe	Val	Arg	Gln	Asp	Asp	Cys	Met	Val

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Leu Lys Glu Phe	290	Leu Arg Ala Asn Ser	295	Pro Thr Met Asp Lys	300
	305		310		315
Leu Ala Asp Ser	Lys	Thr Ala Gln Glu	Ala	Phe Glu Ser Val	Val
	320		325		330
Glu Tyr Phe Gly	Glu	Asn Pro Lys Thr	Thr	Ser Pro Gly Leu	Phe
	335		340		345
Phe Ser Leu Phe	Ser	Arg Phe Ile Lys	Ala	Tyr Lys Lys Ala	Glu
	350		355		360
Gln Glu Val Glu	Gln	Trp Lys Lys Glu	Ala	Ala Ala Gln Glu	Ala
	365		370		375
Gly Ala Asp Thr	Pro	Gly Lys Gly Glu	Pro	Pro Ala Pro Lys	Ser
	380		385		390
Pro Pro Lys Ala	Arg	Arg Pro Gln Met	Asp	Leu Ile Ser Glu	Leu
	395		400		405
Lys Arg Arg Gln	Gln	Lys Glu Pro Leu	Ile	Tyr Glu Ser Asp	Arg
	410		415		420
Asp Gly Ala Ile	Glu	Asp Ile Ile Thr	Asp	Leu Arg Asn Gln	Pro
	425		430		435
Tyr Ile Arg Ala	Asp	Thr Gly Arg Arg	Ser	Ala Arg Arg Arg	Pro
	440		445		450
Pro Gly Pro Pro	Leu	Gln Val Thr Ser	Asp	Leu Ser Leu	
	455		460		

<210> 9
 <211> 270
 <212> PRT
 <213> Homo sapiens

 <220>
 <221> misc_feature
 <223> Incyte ID No: 1988468CD1

 <400> 9
 Met Ala Asp His Met Met Ala Met Asn His Gly Arg Phe Pro Asp
 1 5 10 15
 Gly Thr Asn Gly Leu His His His Pro Ala His Arg Met Gly Met
 20 25 30
 Gly Gln Phe Pro Ser Pro His His His Gln Gln Gln Pro Gln
 35 40 45
 His Ala Phe Asn Ala Leu Met Gly Glu His Ile His Tyr Gly Ala
 50 55 60
 Gly Asn Met Asn Ala Thr Ser Gly Ile Arg His Ala Met Gly Pro
 65 70 75
 Gly Thr Val Asn Gly Gly His Pro Pro Ser Ala Leu Ala Pro Ala
 80 85 90
 Ala Arg Phe Asn Asn Ser Gln Phe Met Gly Pro Pro Val Ala Ser
 95 100 105
 Gln Gly Gly Ser Leu Pro Ala Ser Met Gln Leu Gln Lys Leu Asn
 110 115 120
 Asn Gln Tyr Phe Asn His His Pro Tyr Pro His Asn His Tyr Met
 125 130 135
 Pro Asp Leu His Pro Ala Ala Gly His Gln Met Asn Gly Thr Asn
 140 145 150
 Gln His Phe Arg Asp Cys Asn Pro Lys His Ser Gly Gly Ser Ser
 155 160 165
 Thr Pro Gly Gly Ser Gly Gly Ser Ser Thr Pro Gly Gly Ser Gly
 170 175 180
 Ser Ser Ser Gly Gly Gly Ala Gly Ser Ser Asn Ser Gly Gly Gly
 185 190 195
 Ser Gly Ser Gly Asn Met Pro Ala Ser Val Ala His Val Pro Ala
 200 205 210
 Ala Met Leu Pro Pro Asn Val Ile Asp Thr Asp Phe Ile Asp Glu
 215 220 225

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Glu	Val	Leu	Met	Ser	Leu	Val	Ile	Glu	Met	Gly	Leu	Asp	Arg	Ile
			230											240
Lys	Glu	Leu	Pro	Glu	Leu	Trp	Leu	Gly	Gln	Asn	Glu	Phe	Asp	Phe
			245											255
Met	Thr	Asp	Phe	Val	Cys	Lys	Gln	Gln	Pro	Ser	Arg	Val	Ser	Cys
			260						265					270

<210> 10
 <211> 255
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2049176CD1

<400> 10
 Met Val Ser Trp Met Ile Ser Arg Ala Val Val Leu Val Phe Gly
 1 5 10 15
 Met Leu Tyr Pro Ala Tyr Tyr Ser Tyr Lys Ala Val Lys Thr Lys
 20 25 30
 Asn Val Lys Glu Tyr Val Arg Trp Met Met Tyr Trp Ile Val Phe
 35 40 45
 Ala Leu Tyr Thr Val Ile Glu Thr Val Ala Asp Gln Thr Val Ala
 50 55 60
 Trp Phe Pro Leu Tyr Tyr Glu Leu Lys Ile Ala Phe Val Ile Trp
 65 70 75
 Leu Leu Ser Pro Tyr Thr Lys Gly Ala Ser Leu Ile Tyr Arg Lys
 80 85 90
 Phe Leu His Pro Leu Leu Ser Ser Lys Glu Arg Glu Ile Asp Asp
 95 100 105
 Tyr Ile Val Gln Ala Lys Glu Arg Gly Tyr Glu Thr Met Val Asn
 110 115 120
 Phe Gly Arg Gln Gly Leu Asn Leu Ala Ala Thr Ala Ala Val Thr
 125 130 135
 Ala Ala Val Lys Ser Gln Gly Ala Ile Thr Glu Arg Leu Arg Ser
 140 145 150
 Phe Ser Met His Asp Leu Thr Thr Ile Gln Gly Asp Glu Pro Val
 155 160 165
 Gly Gln Arg Pro Tyr Gln Pro Leu Pro Glu Ala Lys Lys Lys Ser
 170 175 180
 Lys Pro Ala Pro Ser Glu Ser Ala Gly Tyr Gly Ile Pro Leu Lys
 185 190 195
 Asp Gly Asp Glu Lys Thr Asp Glu Glu Ala Glu Gly Pro Tyr Ser
 200 205 210
 Asp Asn Glu Met Leu Thr His Lys Gly Leu Arg Arg Ser Gln Ser
 215 220 225
 Met Lys Ser Val Lys Thr Thr Lys Gly Arg Lys Glu Val Arg Tyr
 230 235 240
 Gly Ser Leu Lys Tyr Lys Val Lys Lys Arg Pro Gln Val Tyr Phe
 245 250 255

<210> 11
 <211> 533
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2686765CD1

<400> 11
 Met Ser Gly Thr Leu Glu Ser Leu Ala Asp Asp Val Ser Ser Met

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1	5	10	15
Gly Ser Asp Ser Glu	Ile Asn Gly Leu Ala	Leu Arg Lys Thr Asp	
20	25	30	
Lys Tyr Gly Phe Leu	Gly Gly Ser Gln Tyr	Ser Gly Ser Leu Glu	
35	40	45	
Ser Ser Ile Pro Val	Asp Val Ala Arg Gln	Arg Glu Leu Lys Trp	
50	55	60	
Leu Asp Met Phe Ser	Asn Trp Asp Lys Trp	Leu Ser Arg Arg Phe	
65	70	75	
Gln Lys Val Lys Leu	Arg Cys Arg Lys Gly	Ile Pro Ser Ser Leu	
80	85	90	
Arg Ala Lys Ala Trp	Gln Tyr Leu Ser Asn	Ser Lys Glu Leu Leu	
95	100	105	
Glu Gln Asn Pro Gly	Lys Phe Glu Glu Leu	Glu Arg Ala Pro Gly	
110	115	120	
Asp Pro Lys Trp Leu	Asp Val Ile Glu Lys	Asp Leu His Arg Gln	
125	130	135	
Phe Pro Phe His Glu	Met Phe Ala Ala Arg	Gly Gly His Gly Gln	
140	145	150	
Gln Asp Leu Tyr Arg	Ile Leu Lys Ala Tyr	Thr Ile Tyr Arg Pro	
155	160	165	
Asp Glu Gly Tyr Cys	Gln Ala Gln Ala Pro	Val Ala Ala Val Leu	
170	175	180	
Leu Met His Met Pro	Ala Glu Lys Pro Phe	Gly Ala Trp Val Gln	
185	190	195	
Ile Cys Asp Lys Tyr	Leu Pro Gly Tyr Tyr	Ser Ala Gly Leu Glu	
200	205	210	
Ala Ile Gln Leu Asp	Gly Glu Ile Phe Phe	Ala Leu Leu Arg Arg	
215	220	225	
Ala Ser Pro Leu Ala	His Arg His Leu Gln	Arg Gln Arg Ile Asp	
230	235	240	
Pro Val Leu Tyr Met	Thr Glu Trp Phe Met	Cys Ile Phe Ala Arg	
245	250	255	
Thr Leu Pro Trp Ala	Ser Val Leu Arg Val	Trp Asp Met Phe Phe	
260	265	270	
Cys Glu Gly Val Lys	Ile Ile Phe Arg Val	Ala Leu Val Leu Leu	
275	280	285	
Arg His Thr Leu Gly	Ser Val Glu Lys Leu	Arg Ser Cys Gln Gly	
290	295	300	
Met Tyr Glu Thr Met	Glu Gln Leu Arg Asn	Leu Pro Gln Gln Cys	
305	310	315	
Met Gln Glu Asp Phe	Leu Val His Glu Val	Thr Asn Leu Pro Val	
320	325	330	
Thr Glu Ala Leu Ile	Glu Arg Glu Asn Ala	Gln Leu Lys Lys	
335	340	345	
Trp Arg Glu Thr Arg	Gly Glu Leu Gln Tyr	Arg Pro Ser Arg Arg	
350	355	360	
Leu His Gly Ser Arg	Ala Ile His Glu Glu	Arg Arg Arg Gln Gln	
365	370	375	
Pro Pro Leu Gly Pro	Ser Ser Ser Leu Leu	Ser Leu Pro Gly Leu	
380	385	390	
Lys Ser Arg Gly Ser	Arg Ala Ala Gly Gly	Ala Pro Ser Pro Pro	
395	400	405	
Pro Pro Val Arg Arg	Ala Ser Ala Gly Pro	Ala Pro Gly Pro Val	
410	415	420	
Val Thr Ala Glu Gly	Leu His Pro Ser Leu	Pro Ser Pro Thr Gly	
425	430	435	
Asn Ser Thr Pro Leu	Gly Ser Ser Lys Glu	Thr Arg Lys Gln Glu	
440	445	450	
Lys Glu Arg Gln Lys	Gln Glu Lys Glu Arg	Gln Lys Gln Glu Lys	
455	460	465	
Glu Arg Glu Lys Glu	Arg Gln Lys Gln Glu	Lys Glu Arg Glu Lys	
470	475	480	

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	95		100		105
Ala Ser Ile Asp Arg	110	Ser Ala Pro Leu Glu	115	Ile Gly Leu Gln Arg	120
Ser Thr Gln Val Lys	125	Arg Ala Ala Asp Glu	130	Val Leu Ala Glu Ala	135
Lys Lys Pro Arg Ile	140	Glu Asp Glu Glu Cys	145	Val Arg Leu Asp Lys	150
Glu Arg Leu Ala Ala	155	Arg Leu Glu Gly His	160	Lys Glu Gly Ile Val	165
Gln Thr Glu Gln Ile	170	Arg Ser Leu Ser Glu	175	Ala Met Ser Val Glu	180
Lys Ile Ala Ala Ile	185	Lys Ala Lys Ile Met	190	Ala Lys Lys Arg Ser	195
Thr Ile Lys Thr Asp	200	Leu Asp Asp Asp Ile	205	Thr Ala Leu Lys Gln	210
Arg Ser Phe Val Asp	215	Ala Glu Val Asp Val	220	Thr Arg Asp Ile Val	225
Ser Arg Glu Arg Val	230	Trp Arg Thr Arg Thr	235	Thr Ile Leu Gln Ser	240
Thr Gly Lys Asn Phe	245	Ser Lys Asn Ile Phe	250	Ala Ile Leu Gln Ser	255
Val Lys Ala Arg Glu	260	Glu Gly Arg Ala Pro	265	Glu Gln Arg Pro Ala	270
Pro Asn Ala Ala Pro	275	Val Asp Pro Thr Leu	280	Arg Thr Lys Gln Pro	285
Ile Pro Ala Ala Tyr	290	Asn Arg Tyr Asp Gln	295	Glu Arg Phe Lys Gly	300
Lys Glu Glu Thr Glu	305	Gly Phe Lys Ile Asp	310	Thr Met Gly Thr Tyr	315
His Gly Met Thr Leu	320	Lys Ser Val Thr Glu	325	Gly Ala Ser Ala Arg	330
Lys Thr Gln Thr Pro	335	Ala Ala Gln Pro Val	340	Pro Arg Pro Val Ser	345
Gln Ala Arg Pro Pro	350	Pro Asn Gln Lys Lys	355	Gly Ser Arg Thr Pro	360
Ile Ile Ile Ile Pro	365	Ala Ala Thr Thr Ser	370	Leu Ile Thr Met Leu	375
Asn Ala Lys Asp Leu	380	Leu Gln Asp Leu Lys	385	Phe Val Pro Ser Asp	390
Glu Lys Lys Lys Gln	395	Gly Cys Gln Arg Glu	400	Asn Glu Thr Leu Ile	405
Gln Arg Arg Lys Asp	410	Gln Met Gln Pro Gly	415	Gly Thr Ala Ile Ser	420
Val Thr Val Pro Tyr	425	Arg Val Val Asp Gln	430	Pro Leu Lys Leu Met	435
Pro Gln Asp Trp Asp	440	Arg Val Val Ala Val	445	Phe Val Gln Gly Pro	450
Ala Trp Gln Phe Lys	455	Gly Trp Pro Trp Leu	460	Leu Pro Asp Gly Ser	465
Pro Val Asp Ile Phe	470	Ala Lys Ile Lys Ala	475	Phe His Leu Lys Tyr	480
Asp Glu Val Arg Leu	485	Asp Pro Asn Val Gln	490	Lys Trp Asp Val Thr	495
Val Leu Glu Leu Ser	500	Tyr His Lys Arg His	505	Leu Asp Arg Pro Val	510
Phe Leu Arg Phe Trp	515	Glu Thr Leu Asp Arg	520	Tyr Met Val Lys His	525
Lys Ser His Leu Arg	530	Phe			

<210> 14

<211> 165

<212> PRT

<213> Homo sapiens

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<220>

<221> misc_feature

<223> Incyte ID No: 5080410CD1

<400> 14

Met	Ala	Ser	Met	Arg	Glu	Ser	Asp	Thr	Gly	Leu	Trp	Leu	His	Asn
1				5					10				15	
Lys	Leu	Gly	Ala	Thr	Asp	Glu	Leu	Trp	Ala	Pro	Pro	Ser	Ile	Ala
				20					25				30	
Ser	Leu	Leu	Thr	Ala	Ala	Val	Ile	Asp	Asn	Ile	Arg	Leu	Cys	Phe
				35					40				45	
His	Gly	Leu	Ser	Ser	Ala	Val	Lys	Leu	Lys	Leu	Leu	Leu	Gly	Thr
				50					55				60	
Leu	His	Leu	Pro	Arg	Arg	Thr	Val	Asp	Glu	His	Pro	Ile	Leu	Pro
				65					70				75	
Met	Lys	Gly	Ala	Leu	Met	Glu	Ile	Ile	Gln	Leu	Ala	Ser	Leu	Asp
				80					85				90	
Ser	Asp	Pro	Trp	Val	Leu	Met	Val	Ala	Asp	Ile	Leu	Lys	Ser	Phe
				95					100				105	
Pro	Asp	Thr	Gly	Ser	Leu	Asn	Leu	Glu	Leu	Glu	Glu	Gln	Asn	Pro
				110					115				120	
Asn	Val	Gln	Asp	Ile	Leu	Gly	Glu	Leu	Arg	Glu	Lys	Val	Gly	Glu
				125					130				135	
Cys	Glu	Ala	Ser	Ala	Met	Leu	Pro	Leu	Glu	Cys	Gln	Tyr	Leu	Asn
				140					145				150	
Lys	Asn	Ala	Ala	Asp	Asp	Pro	Arg	Gly	Thr	Pro	His	Ser	Pro	Gly
				155					160				165	

<210> 15

<211> 199

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5218248CD1

<400> 15

Met	Ser	Asn	Met	Glu	Lys	His	Leu	Phe	Asn	Leu	Lys	Phe	Ala	Ala
1				5					10				15	
Lys	Glu	Leu	Ser	Arg	Ser	Ala	Lys	Lys	Cys	Asp	Lys	Glu	Glu	Lys
				20					25				30	
Ala	Glu	Lys	Ala	Lys	Ile	Lys	Lys	Ala	Ile	Gln	Lys	Gly	Asn	Met
				35					40				45	
Glu	Val	Ala	Arg	Ile	His	Ala	Glu	Asn	Ala	Ile	Arg	Gln	Lys	Asn
				50					55				60	
Gln	Ala	Val	Asn	Phe	Leu	Arg	Met	Ser	Ala	Arg	Val	Asp	Ala	Val
				65					70				75	
Ala	Ala	Arg	Val	Gln	Thr	Ala	Val	Thr	Met	Gly	Lys	Val	Thr	Lys
				80					85				90	
Ser	Met	Ala	Gly	Val	Val	Lys	Ser	Met	Asp	Ala	Thr	Leu	Lys	Thr
				95					100				105	
Met	Asn	Leu	Glu	Lys	Ile	Ser	Ala	Leu	Met	Asp	Lys	Phe	Glu	His
				110					115				120	
Gln	Phe	Glu	Thr	Leu	Asp	Val	Gln	Thr	Gln	Gln	Met	Glu	Asp	Thr
				125					130				135	
Met	Ser	Ser	Thr	Thr	Thr	Leu	Thr	Thr	Pro	Gln	Asn	Gln	Val	Asp
				140					145				150	
Met	Leu	Leu	Gln	Glu	Met	Ala	Asp	Glu	Ala	Gly	Leu	Asp	Leu	Asn
				155					160				165	
Met	Glu	Leu	Pro	Gln	Gly	Gln	Thr	Gly	Ser	Val	Gly	Thr	Ser	Val
				170					175				180	
Ala	Ser	Ala	Glu	Gln	Asp	Glu	Leu	Ser	Gln	Arg	Leu	Ala	Arg	Leu

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Arg Asp Gln Val 185 190 195

<210> 16
 <211> 168
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 058336CD1

<400> 16
 Met Ala Phe Asn Asp Cys Phe Ser Leu Asn Tyr Pro Gly Asn Pro
 1 5 10 15
 Cys Pro Gly Asp Leu Ile Glu Val Phe Arg Pro Gly Tyr Gln His
 20 25 30
 Trp Ala Leu Tyr Leu Gly Asp Gly Tyr Val Ile Asn Ile Ala Pro
 35 40 45
 Val Asp Gly Ile Pro Ala Ser Phe Thr Ser Ala Lys Ser Val Phe
 50 55 60
 Ser Ser Lys Ala Leu Val Lys Met Gln Leu Leu Lys Asp Val Val
 65 70 75
 Gly Asn Asp Thr Tyr Arg Ile Asn Asn Lys Tyr Asp Glu Thr Tyr
 80 85 90
 Pro Pro Leu Pro Val Glu Glu Ile Ile Lys Arg Ser Glu Phe Val
 95 100 105
 Ile Gly Gln Glu Val Ala Tyr Asn Leu Leu Val Asn Asn Cys Glu
 110 115 120
 His Phe Val Thr Leu Leu Arg Tyr Gly Glu Gly Val Ser Glu Gln
 125 130 135
 Ala Asn Arg Ala Ile Ser Thr Val Glu Phe Val Thr Ala Ala Val
 140 145 150
 Gly Val Phe Ser Phe Leu Gly Leu Phe Pro Lys Gly Gln Arg Ala
 155 160 165

Lys Tyr Tyr

<210> 17
 <211> 162
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 1511488CD1

<400> 17
 Met Leu Arg Ala Val Gly Ser Leu Leu Arg Leu Gly Arg Gly Leu
 1 5 10 15
 Thr Val Arg Cys Gly Pro Gly Ala Pro Leu Glu Ala Thr Arg Arg
 20 25 30
 Pro Ala Pro Ala Leu Pro Pro Arg Gly Leu Pro Cys Tyr Ser Ser
 35 40 45
 Gly Gly Ala Pro Ser Asn Ser Gly Pro Gln Gly His Gly Glu Ile
 50 55 60
 His Arg Val Pro Thr Gln Arg Arg Pro Ser Gln Phe Asp Lys Lys
 65 70 75
 Ile Leu Leu Trp Thr Gly Arg Phe Lys Ser Met Glu Glu Ile Pro
 80 85 90
 Pro Arg Ile Pro Pro Glu Met Ile Asp Thr Ala Arg Asn Lys Ala
 95 100 105
 Arg Val Lys Ala Cys Tyr Ile Met Ile Gly Leu Thr Ile Ile Ala
 110 115 120

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Cys Phe Ala Val Ile Val Ser Ala Lys Arg Ala Val Glu Arg His
 125 130 135
 Glu Ser Leu Thr Ser Trp Asn Leu Ala Lys Lys Ala Lys Trp Arg
 140 145 150
 Glu Glu Ala Ala Leu Ala Ala Gln Ala Lys Ala Lys
 155 160

<210> 18
 <211> 246
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 1638819CD1

<400> 18
 Met Ala Gly Tyr Leu Lys Leu Val Cys Val Ser Phe Gln Arg Gln
 1 5 10 15
 Gly Phe His Thr Val Gly Ser Arg Cys Lys Asn Arg Thr Gly Ala
 20 25 30
 Glu His Leu Trp Leu Thr Arg His Leu Arg Asp Pro Phe Val Lys
 35 40 45
 Ala Ala Lys Val Glu Ser Tyr Arg Cys Arg Ser Ala Phe Lys Leu
 50 55 60
 Leu Glu Val Asn Glu Arg His Gln Ile Leu Arg Pro Gly Leu Arg
 65 70 75
 Val Leu Asp Cys Gly Ala Ala Pro Gly Ala Trp Ser Gln Val Ala
 80 85 90
 Val Gln Lys Val Asn Ala Ala Gly Thr Asp Pro Ser Ser Pro Val
 95 100 105
 Gly Phe Val Leu Gly Val Asp Leu Leu His Ile Phe Pro Leu Glu
 110 115 120
 Gly Ala Thr Phe Leu Cys Pro Ala Asp Val Thr Asp Pro Arg Thr
 125 130 135
 Ser Gln Arg Ile Leu Glu Val Leu Pro Gly Arg Arg Ala Asp Val
 140 145 150
 Ile Leu Ser Asp Met Ala Pro Asn Ala Thr Gly Phe Arg Asp Leu
 155 160 165
 Asp His Asp Arg Leu Ile Ser Leu Cys Leu Thr Leu Leu Ser Val
 170 175 180
 Thr Pro Asp Ile Leu Gln Pro Gly Gly Thr Phe Leu Cys Lys Thr
 185 190 195
 Trp Ala Gly Ser Gln Ser Arg Arg Leu Gln Arg Arg Leu Thr Glu
 200 205 210
 Glu Phe Gln Asn Val Arg Ile Ile Lys Pro Glu Ala Ser Arg Lys
 215 220 225
 Glu Ser Ser Glu Val Tyr Phe Leu Ala Thr Gln Tyr His Gly Arg
 230 235 240
 Lys Gly Thr Val Lys Gln
 245

<210> 19
 <211> 483
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 1655123CD1

<400> 19
 Met Glu Glu Gly Gly Gly Val Arg Ser Leu Val Pro Gly Gly
 1 5 10 15
 Pro Val Leu Leu Val Leu Cys Gly Leu Leu Glu Ala Ser Gly Gly

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	20		25		30
Gly Arg Ala Leu Pro	Gln Leu Ser Asp	Asp	Ile Pro Phe Arg	Val	
	35		40		45
Asn Trp Pro Gly Thr	Glu Phe Ser Leu	Pro	Thr Thr Gly Val	Leu	
	50		55		60
Tyr Lys Glu Asp Asn	Tyr Val Ile Met	Thr	Thr Ala His Lys	Glu	
	65		70		75
Lys Tyr Lys Cys Ile	Leu Pro Leu Val	Thr	Ser Gly Asp Glu	Glu	
	80		85		90
Glu Glu Lys Asp Tyr	Lys Gly Pro Asn	Pro	Arg Glu Leu Leu	Glu	
	95		100		105
Pro Leu Phe Lys Gln	Ser Ser Cys Ser	Tyr	Arg Ile Glu Ser	Tyr	
	110		115		120
Trp Thr Tyr Glu Val	Cys His Gly Lys	His	Ile Arg Gln Tyr	His	
	125		130		135
Glu Glu Lys Glu Thr	Gly Gln Lys Ile	Asn	Ile His Glu Tyr	Tyr	
	140		145		150
Leu Gly Asn Met Leu	Ala Lys Asn Leu	Leu	Phe Glu Lys Glu	Arg	
	155		160		165
Glu Ala Glu Glu Lys	Glu Lys Ser Asn	Glu	Ile Pro Thr Lys	Asn	
	170		175		180
Ile Glu Gly Gln Met	Thr Pro Tyr Tyr	Pro	Val Gly Met Gly	Asn	
	185		190		195
Gly Thr Pro Cys Ser	Leu Lys Gln Asn	Arg	Pro Arg Ser Ser	Thr	
	200		205		210
Val Met Tyr Ile Cys	His Pro Glu Ser	Lys	His Glu Ile Leu	Ser	
	215		220		225
Val Ala Glu Val Thr	Thr Cys Glu Tyr	Glu	Val Val Ile Leu	Thr	
	230		235		240
Pro Leu Leu Cys Ser	His Pro Lys Tyr	Arg	Phe Arg Ala Ser	Pro	
	245		250		255
Val Asn Asp Ile Phe	Cys Gln Ser Leu	Pro	Gly Ser Pro Phe	Lys	
	260		265		270
Pro Leu Thr Leu Arg	Gln Leu Glu Gln	Glu	Glu Ile Leu Arg		
	275		280		285
Val Pro Phe Arg Arg	Asn Lys Glu Glu	Asp	Leu Gln Ser Thr	Lys	
	290		295		300
Glu Glu Arg Phe Pro	Ala Ile His Lys	Ser	Ile Ala Ile Gly	Ser	
	305		310		315
Gln Pro Val Leu Thr	Val Gly Thr Thr	His	Ile Ser Lys Leu	Thr	
	320		325		330
Asp Asp Gln Leu Ile	Lys Glu Phe Leu	Ser	Gly Ser Tyr Cys	Phe	
	335		340		345
Arg Gly Gly Val Gly	Trp Trp Lys Tyr	Glu	Phe Cys Tyr Gly	Lys	
	350		355		360
His Val His Gln Tyr	His Glu Asp Lys	Asp	Ser Gly Lys Thr	Ser	
	365		370		375
Val Val Val Gly Thr	Trp Asn Gln Glu	Glu	His Ile Glu Trp	Ala	
	380		385		390
Lys Lys Asn Thr Ala	Arg Ala Tyr His	Leu	Gln Asp Asp Gly	Thr	
	395		400		405
Gln Thr Val Arg Met	Val Ser His Phe	Tyr	Gly Asn Gly Asp	Ile	
	410		415		420
Cys Asp Ile Thr Asp	Lys Pro Arg Gln	Val	Thr Val Lys Leu	Lys	
	425		430		435
Cys Lys Glu Ser Asp	Ser Pro His Ala	Val	Thr Val Tyr Met	Leu	
	440		445		450
Glu Pro His Ser Cys	Gln Tyr Ile Leu	Gly	Val Glu Ser Pro	Val	
	455		460		465
Ile Cys Lys Ile Leu	Asp Thr Ala Asp	Glu	Asn Gly Leu Leu	Ser	
	470		475		480
Leu Pro Asn					

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<210> 20
 <211> 280
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2553926CD1

<400> 20
 Met Glu Ala Ala Glu Thr Glu Ala Glu Ala Ala Ala Leu Glu Val
 1 5 10 15
 Leu Ala Glu Val Ala Gly Ile Leu Glu Pro Val Gly Leu Gln Glu
 20 25 30
 Glu Ala Glu Leu Pro Ala Lys Ile Leu Val Glu Phe Val Val Asp
 35 40 45
 Ser Gln Lys Lys Asp Lys Leu Leu Cys Ser Gln Leu Gln Val Ala
 50 55 60
 Asp Phe Leu Gln Asn Ile Leu Ala Gln Glu Asp Thr Ala Lys Gly
 65 70 75
 Leu Asp Pro Leu Ala Ser Glu Asp Thr Ser Arg Gln Lys Ala Ile
 80 85 90
 Ala Ala Lys Glu Gln Trp Lys Glu Leu Lys Ala Thr Tyr Arg Glu
 95 100 105
 His Val Glu Ala Ile Lys Ile Gly Leu Thr Lys Ala Leu Thr Gln
 110 115 120
 Met Glu Glu Ala Gln Arg Lys Arg Thr Gln Leu Arg Glu Ala Phe
 125 130 135
 Glu Gln Leu Gln Ala Lys Lys Gln Met Ala Met Glu Lys Arg Arg
 140 145 150
 Ala Val Gln Asn Gln Trp Gln Leu Gln Gln Glu Lys His Leu Gln
 155 160 165
 His Leu Ala Glu Val Ser Ala Glu Val Arg Glu Arg Lys Thr Gly
 170 175 180
 Thr Gln Gln Glu Leu Asp Gly Val Phe Gln Lys Leu Gly Asn Leu
 185 190 195
 Lys Gln Gln Ala Glu Gln Glu Arg Asp Lys Leu Gln Arg Tyr Gln
 200 205 210
 Thr Phe Leu Gln Leu Leu Tyr Thr Leu Gln Gly Lys Leu Leu Phe
 215 220 225
 Pro Glu Ala Glu Ala Glu Ala Glu Asn Leu Pro Asp Asp Lys Pro
 230 235 240
 Gln Gln Pro Thr Arg Pro Gln Glu Gln Ser Thr Gly Asp Thr Met
 245 250 255
 Gly Arg Asp Pro Gly Val Ser Phe Lys Phe Ser Lys Ala Val Gly
 260 265 270
 Leu Gln Pro Ala Gly Asp Val Asn Leu Pro
 275 280

<210> 21
 <211> 425
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2800717CD1

<400> 21
 Met Gly Glu Asp Ala Ala Gln Ala Glu Lys Phe Gln His Pro Gly
 1 5 10 15
 Ser Asp Met Arg Gln Glu Lys Pro Ser Ser Pro Ser Pro Met Pro
 20 25 30
 Ser Ser Thr Pro Ser Pro Ser Leu Asn Leu Gly Asn Thr Glu Glu

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	35		40		45
Ala Ile Arg Asp Asn	Ser Gln Val Asn	Ala Val Thr Val Leu Thr			
Leu Leu Asp Lys Leu	Val Asn Met Leu Asp	Ala Val Gln Glu Asn			
Gln His Lys Met Glu	Gln Arg Gln Ile Ser	Leu Glu Gly Ser Val			
Lys Gly Ile Gln Asn	Asp Leu Thr Lys	Leu Ser Lys Tyr Gln Ala			
Ser Thr Ser Asn Thr	Val Ser Lys Leu	Leu Glu Lys Ser Arg Lys			
Val Ser Ala His Thr	Arg Ala Val Lys	Glu Arg Met Asp Arg Gln			
Cys Ala Gln Val Lys	Arg Leu Glu Asn	Asn His Ala Gln Leu Leu			
Arg Arg Asn His Phe	Lys Val Leu Ile	Phe Gln Glu Glu Asn Glu			
Ile Pro Ala Ser Val	Phe Val Lys Gln	Pro Val Ser Gly Ala Val			
Glu Gly Lys Glu Glu	Leu Pro Asp Glu	Asn Lys Ser Leu Glu Glu			
Thr Leu His Thr Val	Asp Leu Ser Ser	Asp Asp Leu Pro His			
Asp Glu Glu Ala Leu	Glu Asp Ser Ala	Glu Lys Val Glu Glu			
Ser Arg Ala Glu Lys	Ile Lys Arg Ser	Ser Leu Lys Lys Val Asp			
Ser Leu Lys Lys Ala	Phe Ser Arg Gln	Asn Ile Glu Lys Lys Met			
Asn Lys Leu Gly Thr	Lys Ile Val Ser	Val Glu Arg Arg Glu Lys			
Ile Lys Lys Ser Leu	Thr Ser Asn His	Gln Lys Ile Ser Ser Gly			
Lys Ser Ser Pro Phe	Lys Val Ser Pro	Leu Thr Phe Gly Arg Lys			
Lys Val Arg Glu Gly	Glu Ser His Ala	Glu Asn Glu Thr Lys Ser			
Glu Asp Leu Pro Ser	Ser Glu Gln Met	Pro Asn Asp Gln Glu Glu			
Glu Ser Phe Ala Glu	Gly His Ser Glu	Ala Ser Leu Ala Ser Ala			
Leu Val Glu Gly Glu	Ile Ala Glu Glu	Ala Glu Lys Ala Thr			
Ser Arg Gly Ser Asn	Ser Gly Met Asp	Ser Asn Ile Asp Leu Thr			
Ile Val Glu Asp Glu	Glu Glu Glu Ser	Val Ala Leu Glu Gln Ala			
Gln Lys Val Arg Tyr	Glu Gly Ser Tyr	Ala Leu Thr Ser Glu Glu			
Ala Glu Arg Ser Asp	Gly Asp Pro Val	Gln Pro Ala Val Leu Gln			
Val His Gln Thr Ser					

<210> 22

<211> 128

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5664154CD1

<400> 22

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Met Glu Ser Lys Glu Glu Arg Ala Leu Asn Asn Leu Ile Val Glu
 1          5          10          15
Asn Val Asn Gln Glu Asn Asp Glu Lys Asp Glu Lys Glu Gln Val
          20          25          30
Ala Asn Lys Gly Glu Pro Leu Ala Leu Pro Leu Asn Val Ser Glu
          35          40          45
Tyr Cys Val Pro Arg Gly Asn Arg Arg Arg Phe Arg Val Arg Gln
          50          55          60
Pro Ile Leu Gln Tyr Arg Trp Asp Ile Met His Arg Leu Gly Glu
          65          70          75
Pro Gln Ala Arg Met Met Arg Glu Glu Asn Met Glu Arg Ile Gly Glu
          80          85          90
Glu Val Arg Gln Leu Met Glu Lys Leu Arg Glu Lys Gln Leu Ser
          95          100          105
His Ser Leu Arg Ala Val Ser Thr Asp Pro Pro His His Asp His
          110          115          120
His Asp Glu Phe Cys Leu Met Pro
          125

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<210> 23
<211> 113
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 017900CD1

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<400> 23
Met Asp Gly Arg Val Gln Leu Ile Lys Ala Leu Leu Ala Leu Pro
 1          5          10          15
Ile Arg Pro Ala Thr Arg Arg Trp Arg Asn Pro Ile Pro Phe Pro
          20          25          30
Glu Thr Phe Asp Gly Asp Thr Asp Arg Leu Pro Glu Phe Ile Val
          35          40          45
Gln Thr Gly Ser Tyr Met Phe Val Asp Glu Asn Thr Phe Ser Ser
          50          55          60
Asp Ala Leu Lys Val Thr Phe Leu Ile Thr Arg Leu Thr Gly Pro
          65          70          75
Ala Leu Gln Trp Val Ile Pro Tyr Ile Lys Lys Glu Ser Pro Leu
          80          85          90
Leu Asn Asp Tyr Arg Gly Phe Leu Ala Glu Met Lys Arg Val Phe
          95          100          105
Gly Trp Glu Glu Asp Glu Asp Phe
          110

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<210> 24
<211> 308
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 035102CD1

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<400> 24
Met Leu Gln Thr Pro Glu Ser Arg Gly Leu Pro Val Pro Gln Ala
 1          5          10          15
Glu Gly Glu Lys Asp Gly Gly His Asp Gly Glu Thr Arg Ala Pro
          20          25          30
Thr Ala Ser Gln Glu Arg Pro Lys Glu Glu Leu Gly Ala Gly Arg
          35          40          45
Glu Glu Gly Ala Ala Glu Pro Ala Leu Thr Arg Lys Gly Ala Arg
          50          55          60
Ala Leu Ala Ala Lys Ser Leu Ala Arg Arg Arg Ala Tyr Arg Arg

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65	70	75
Leu Asn Arg Thr Val	Ala Glu Leu Val Gln	Phe Leu Leu Val Lys
80	85	90
Asp Lys Lys Lys Ser	Pro Ile Thr Arg Ser	Glu Met Val Lys Tyr
95	100	105
Val Ile Gly Asp Leu	Lys Ile Leu Phe Pro	Asp Ile Ile Ala Arg
110	115	120
Ala Ala Glu His Leu	Arg Tyr Val Phe Gly	Phe Glu Leu Lys Gln
125	130	135
Phe Asp Arg Lys His	His Thr Tyr Ile Leu	Ile Asn Lys Leu Lys
140	145	150
Pro Leu Glu Glu Glu	Glu Glu Glu Glu Asp	Leu Gly Gly Asp Gly
155	160	165
Pro Arg Leu Gly Leu	Leu Met Met Ile Leu	Gly Leu Ile Tyr Met
170	175	180
Arg Gly Asn Ser Ala	Arg Glu Ala Gln Val	Trp Glu Met Leu Arg
185	190	195
Arg Leu Gly Val Gln	Pro Ser Lys Tyr His	Phe Leu Phe Gly Tyr
200	205	210
Pro Lys Arg Leu Ile	Met Glu Asp Phe Val	Gln Gln Arg Tyr Leu
215	220	225
Ser Tyr Arg Arg Val	Pro His Thr Asn Pro	Pro Ala Tyr Glu Phe
230	235	240
Ser Trp Gly Pro Arg	Ser Asn Leu Glu Ile	Ser Lys Met Glu Val
245	250	255
Leu Gly Phe Val Ala	Lys Leu His Lys Lys	Glu Pro Gln His Trp
260	265	270
Pro Val Gln Tyr Arg	Glu Ala Leu Ala Asp	Glu Ala Asp Arg Ala
275	280	285
Arg Ala Lys Ala Arg	Ala Glu Ala Ser Met	Arg Ala Arg Ala Ser
290	295	300
Ala Arg Ala Gly Ile	His Leu Trp	
305		

<210> 25

<211> 221

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 259983CD1

<400> 25

Met Phe Gly Phe His	Lys Pro Lys Met Tyr	Arg Ser Ile Glu Gly
1	5	10
Cys Cys Ile Cys Arg	Ala Lys Ser Ser Ser	Ser Arg Phe Thr Asp
20	25	30
Ser Lys Arg Tyr Glu	Lys Asp Phe Gln Ser	Cys Phe Gly Leu His
35	40	45
Glu Thr Arg Ser Gly	Asp Ile Cys Asn Ala	Cys Val Leu Leu Val
50	55	60
Lys Arg Trp Lys Lys	Leu Pro Ala Gly Ser	Lys Lys Asn Trp Asn
65	70	75
His Val Val Asp Ala	Arg Ala Gly Pro Ser	Leu Lys Thr Thr Leu
80	85	90
Lys Pro Lys Lys Val	Lys Thr Leu Ser Gly	Asn Arg Ile Lys Ser
95	100	105
Asn Gln Ile Ser Lys	Leu Gln Lys Glu Phe	Lys Arg His Asn Ser
110	115	120
Asp Ala His Ser Thr	Thr Ser Ser Ala Ser	Pro Ala Gln Ser Pro
125	130	135
Cys Tyr Ser Asn Gln	Ser Asp Asp Gly Ser	Asp Thr Glu Met Ala
140	145	150

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Ser	Gly	Ser	Asn	Arg	Thr	Pro	Val	Phe	Ser	Phe	Leu	Asp	Leu	Thr	
			155						160					165	
Tyr	Trp	Lys	Arg	Gln	Lys	Ile	Cys	Cys	Gly	Ile	Ile	Tyr	Lys	Gly	
			170						175					180	
Arg	Phe	Gly	Glu	Val	Leu	Ile	Asp	Thr	His	Leu	Phe	Lys	Pro	Cys	
			185						190					195	
Cys	Ser	Asn	Lys	Lys	Ala	Ala	Ala	Glu	Lys	Pro	Glu	Glu	Gln	Gly	
			200						205					210	
Pro	Glu	Pro	Leu	Pro	Ile	Ser	Thr	Gln	Glu	Trp					
			215						220						

<210> 26

<211> 402

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 926810CD1

<400> 26

Met	Ala	Ser	Ile	Ile	Ala	Arg	Val	Gly	Asn	Ser	Arg	Arg	Leu	Asn	
1			5						10					15	
Ala	Pro	Leu	Pro	Pro	Trp	Ala	His	Ser	Met	Leu	Arg	Ser	Leu	Gly	
			20						25					30	
Arg	Ser	Leu	Gly	Pro	Ile	Met	Ala	Ser	Met	Ala	Asp	Arg	Asn	Met	
			35						40					45	
Lys	Leu	Phe	Ser	Gly	Arg	Val	Val	Pro	Ala	Gln	Gly	Glu	Glu	Thr	
			50						55					60	
Phe	Glu	Asn	Trp	Leu	Thr	Gln	Val	Asn	Gly	Val	Leu	Pro	Asp	Trp	
			65						70					75	
Asn	Met	Ser	Glu	Glu	Glu	Lys	Leu	Lys	Arg	Leu	Met	Lys	Thr	Leu	
			80						85					90	
Arg	Gly	Pro	Ala	Arg	Glu	Val	Met	Arg	Val	Leu	Gln	Ala	Thr	Asn	
			95						100					105	
Pro	Asn	Leu	Ser	Val	Ala	Asp	Phe	Leu	Arg	Ala	Met	Lys	Leu	Val	
			110						115					120	
Phe	Gly	Glu	Ser	Glu	Ser	Ser	Val	Thr	Ala	His	Gly	Lys	Phe	Phe	
			125						130					135	
Asn	Thr	Leu	Gln	Ala	Gln	Gly	Glu	Lys	Ala	Ser	Leu	Tyr	Val	Ile	
			140						145					150	
Arg	Leu	Glu	Val	Gln	Leu	Gln	Asn	Ala	Ile	Gln	Ala	Gly	Ile	Ile	
			155						160					165	
Ala	Glu	Lys	Asp	Ala	Asn	Arg	Thr	Arg	Leu	Gln	Gln	Leu	Leu	Leu	
			170						175					180	
Gly	Gly	Glu	Leu	Ser	Arg	Asp	Leu	Arg	Leu	Arg	Leu	Lys	Asp	Phe	
			185						190					195	
Leu	Arg	Met	Tyr	Ala	Asn	Glu	Gln	Glu	Arg	Leu	Pro	Asn	Phe	Leu	
			200						205					210	
Glu	Leu	Ile	Arg	Met	Val	Arg	Glu	Glu	Glu	Asp	Trp	Asp	Asp	Ala	
			215						220					225	
Phe	Ile	Lys	Arg	Lys	Arg	Pro	Lys	Arg	Ser	Glu	Ser	Met	Val	Glu	
			230						235					240	
Arg	Ala	Val	Ser	Pro	Val	Ala	Phe	Gln	Gly	Ser	Pro	Pro	Ile	Val	
			245						250					255	
Ile	Gly	Ser	Ala	Asp	Cys	Asn	Val	Ile	Glu	Ile	Asp	Asp	Thr	Leu	
			260						265					270	
Asp	Asp	Ser	Asp	Glu	Asp	Val	Ile	Leu	Val	Glu	Ser	Gln	Asp	Pro	
			275						280					285	
Pro	Leu	Pro	Ser	Trp	Gly	Ala	Pro	Pro	Leu	Arg	Asp	Arg	Ala	Arg	
			290						295					300	
Pro	Gln	Asp	Glu	Val	Leu	Val	Ile	Asp	Ser	Pro	His	Asn	Ser	Arg	
			305						310					315	
Ala	Gln	Phe	Pro	Ser	Thr	Ser	Gly	Gly	Ser	Gly	Tyr	Lys	Asn	Asn	

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Gly	Pro	Gly	Glu	Met	Arg	Arg	Ala	Arg	Lys	Arg	Lys	His	Thr	Ile
320									325					330
335									340					345
Arg	Cys	Ser	Tyr	Cys	Gly	Glu	Glu	Gly	His	Ser	Lys	Glu	Thr	Cys
350									355					360
Asp	Asn	Glu	Ser	Asp	Lys	Ala	Gln	Val	Phe	Glu	Asn	Leu	Ile	Ile
365									370					375
Thr	Leu	Gln	Glu	Leu	Thr	His	Thr	Glu	Met	Glu	Arg	Ser	Arg	Val
380									385					390
Ala	Pro	Gly	Glu	Tyr	Asn	Asp	Phe	Ser	Glu	Pro	Leu			
395									400					

<210> 27

<211> 93

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1398816CD1

<400> 27

Met	Ser	Thr	Asp	Thr	Gly	Val	Ser	Leu	Pro	Ser	Tyr	Glu	Glu	Asp
1					5				10					15
Gln	Gly	Ser	Lys	Leu	Ile	Arg	Lys	Ala	Lys	Glu	Ala	Pro	Phe	Val
20									25					30
Pro	Val	Gly	Ile	Ala	Gly	Phe	Ala	Ala	Ile	Val	Ala	Tyr	Gly	Leu
35									40					45
Tyr	Lys	Leu	Lys	Ser	Arg	Gly	Asn	Thr	Lys	Met	Ser	Ile	His	Leu
50									55					60
Ile	His	Met	Arg	Val	Ala	Ala	Gln	Gly	Phe	Val	Val	Gly	Ala	Met
65									70					75
Thr	Val	Gly	Met	Gly	Tyr	Ser	Met	Tyr	Arg	Glu	Phe	Trp	Ala	Lys
80									85					90

Pro Lys Pro

<210> 28

<211> 353

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1496820CD1

<400> 28

Met	Asn	Arg	Glu	Asp	Arg	Asn	Val	Leu	Arg	Met	Lys	Glu	Arg	Glu
1					5				10					15
Arg	Arg	Asn	Gln	Glu	Ile	Gln	Gln	Gly	Glu	Asp	Ala	Phe	Pro	Pro
20									25					30
Ser	Ser	Pro	Leu	Phe	Ala	Glu	Pro	Tyr	Lys	Val	Thr	Ser	Lys	Glu
35									40					45
Asp	Lys	Leu	Ser	Ser	Arg	Ile	Gln	Ser	Met	Leu	Gly	Asn	Tyr	Asp
50									55					60
Glu	Met	Lys	Asp	Phe	Ile	Gly	Asp	Arg	Ser	Ile	Pro	Lys	Leu	Val
65									70					75
Ala	Ile	Pro	Lys	Pro	Thr	Val	Pro	Pro	Ser	Ala	Asp	Glu	Lys	Ser
80									85					90
Asn	Pro	Asn	Phe	Phe	Glu	Gln	Arg	His	Gly	Gly	Ser	His	Gln	Ser
95									100					105
Ser	Lys	Trp	Thr	Pro	Val	Gly	Pro	Ala	Pro	Ser	Thr	Ser	Gln	Ser
110									115					120
Gln	Lys	Arg	Ser	Ser	Gly	Leu	Gln	Ser	Gly	His	Ser	Ser	Gln	Arg
125									130					135

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Thr	Ser	Ala	Gly	Ser	Ser	Ser	Gly	Thr	Asn	Ser	Ser	Gly	Gln	Arg	
				140					145					150	
His	Asp	Arg	Glu	Ser	Tyr	Asn	Asn	Ser	Gly	Ser	Ser	Ser	Arg	Lys	
				155					160					165	
Lys	Gly	Gln	His	Gly	Ser	Glu	His	Ser	Lys	Ser	Arg	Ser	Ser	Ser	
				170					175					180	
Pro	Gly	Lys	Pro	Gln	Ala	Val	Ser	Ser	Leu	Asn	Ser	Ser	His	Ser	
				185					190					195	
Arg	Ser	His	Gly	Asn	Asp	His	His	Ser	Lys	Glu	His	Gln	Arg	Ser	
				200					205					210	
Lys	Ser	Pro	Arg	Asp	Pro	Asp	Ala	Asn	Trp	Asp	Ser	Pro	Ser	Arg	
				215					220					225	
Val	Pro	Phe	Ser	Ser	Gly	Gln	His	Ser	Thr	Gln	Ser	Phe	Pro	Pro	
				230					235					240	
Ser	Leu	Met	Ser	Lys	Ser	Asn	Ser	Met	Leu	Gln	Lys	Pro	Thr	Ala	
				245					250					255	
Tyr	Val	Arg	Pro	Met	Asp	Gly	Gln	Glu	Ser	Met	Glu	Pro	Lys	Leu	
				260					265					270	
Ser	Ser	Glu	His	Tyr	Ser	Ser	Gln	Ser	His	Gly	Asn	Ser	Met	Thr	
				275					280					285	
Glu	Leu	Lys	Pro	Ser	Ser	Lys	Ala	His	Leu	Thr	Lys	Leu	Lys	Ile	
				290					295					300	
Pro	Ser	Gln	Pro	Leu	Asp	Ala	Ser	Ala	Ser	Gly	Asp	Val	Ser	Cys	
				305					310					315	
Val	Asp	Glu	Ile	Leu	Lys	Glu	Met	Thr	His	Ser	Trp	Pro	Pro	Pro	
				320					325					330	
Leu	Thr	Ala	Ile	His	Thr	Pro	Cys	Lys	Thr	Glu	Pro	Ser	Lys	Phe	
				335					340					345	
Pro	Phe	Pro	Thr	Lys	Val	Ser	Lys								
				350											

<210> 29

<211> 120

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1514559CD1

<400> 29

Met	Ser	Glu	Pro	Ala	Gly	Asp	Val	Arg	Gln	Asn	Pro	Cys	Gly	Ser	
				5					10					15	
Lys	Ala	Cys	Arg	Arg	Leu	Phe	Gly	Pro	Val	Asp	Ser	Glu	Gln	Leu	
				20					25					30	
Ser	Arg	Asp	Cys	Asp	Ala	Leu	Met	Ala	Gly	Cys	Ile	Gln	Glu	Ala	
				35					40					45	
Arg	Glu	Arg	Trp	Asn	Phe	Asp	Phe	Val	Thr	Glu	Thr	Pro	Leu	Glu	
				50					55					60	
Gly	Asp	Phe	Ala	Trp	Glu	Arg	Val	Arg	Gly	Leu	Gly	Leu	Pro	Lys	
				65					70					75	
Leu	Tyr	Leu	Pro	Thr	Trp	Ser	Ala	Gly	Trp	Tyr	Pro	Leu	Glu	Gly	
				80					85					90	
Cys	Gly	Ser	Phe	Pro	Ser	Leu	Ser	Gln	Ala	Val	Met	Lys	Phe	Thr	
				95					100					105	
Pro	Phe	Pro	Gly	His	Ser	Asp	Leu	Asn	Ser	Phe	Ser	Phe	Glu	Lys	
				110					115					120	

<210> 30

<211> 144

<212> PRT

<213> Homo sapiens

<220>

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Asp	Asp	Lys	Gly	215	Ala	Gln	Ala	Ala	Arg	220	Gly	Ser	Ser	Asn	Ala	225
Leu	Lys	Glu	Glu	230	Cys	Lys	Glu	Pro	Leu	235	Leu	Phe	His	Ser	Gly	240
Asp	His	Tyr	Pro	245	Leu	Ser	Asp	Gly	Asp	250	Trp	Ser	Pro	Leu	Glu	255
Thr	Tyr	Pro	Gln	260	Thr	Ala	Cys	Pro	Lys	265	Ser	Asp	Ser	Glu	Leu	270
Val	Lys	Pro	Ala	275	Glu	Ser	Leu	Leu	Arg	280	Ser	Glu	Tyr	His	Met	285
Trp	Thr	Trp	Gly	290	Gly	Phe	Pro	Glu	Ser	295	Thr	Lys	Val	Ser	Lys	300
Glu	Arg	Ser	Asp	305	His	His	Pro	Arg	Thr	310	Ala	Thr	Ile	Thr	Pro	315
Glu	Asn	Thr	His	320	Phe	Arg	Val	Ile	Pro	325	Ser	Glu	Asp	Asn	Leu	330
Ser	Glu	Val	Glu	335	Lys	Asp	Ala	Ser	Met	340	Glu	Asp	Thr	Val	Cys	345
Ile	Val	Lys	Pro	350	Lys	Pro	Arg	Ala	Leu	355	Gly	Thr	Gln	Met	Ser	360
Pro	Thr	Ser	Val	365	Lys	Pro	Arg	Ala	Leu	370	Gly	Thr	Gln	Met	Ser	375
Gln	Ile	Ser	Ser	380	Glu	Leu	Leu	Glu	Pro	385	Pro	Leu	Glu	Ser	Thr	390
Leu	Ala	Glu	Ala	395	Met	Leu	Asp	Ala	Asp	400	His	Leu	Pro	Asn	Ala	405
Ser	Pro	Ser	Lys	410	Pro	Ser	Glu	Ser	Lys	415	Pro	Ala	Ala	Lys	Val	420
Gly	Pro	Asp	Asp	425	Lys	Lys	Gly	Val	His	430	Lys	Arg	Ile	Gln	His	435
Glu	Val	Ala	Ala	440	Ile	Tyr	Leu	Asp	Asp	445	Leu	Lys	Gly	Leu	Glu	450
Ser	Arg	Gln	Trp	455	Thr	Phe	Pro	Lys	Ser	460	Glu	Ser	Glu	Pro	Gly	465
Pro	Gln	Ser	Val	470	Pro	Glu	Ser	Asp	Thr	475	Leu	Ser	Gly	Ser	Gln	480
Leu	Ser	Asp	Ser	485	Gly	Ser	Ala	Ala	Ala	490	Asp	Ser	Gly	Thr	Glu	495
Cys	Gly	Gly	Leu	500	Ala	Met	Asp	Leu	Pro	505	Asp	Val	Thr	Leu	Ser	510
Met	Glu	His	Ile	515	Ser	Glu	Asn	Gly	Lys	520	Ile	Ser	Lys	Glu	Lys	525
Leu	Ile	Asp	Asn	530	Ile	Thr	Tyr	His	Glu	535	Phe	Ala	Glu	Asn	Pro	540
Tyr	Asn	Trp	Ala	545	Pro	Asn	Leu	Val	Ile	550	Arg	Ile	Tyr	Asn	Arg	555
Phe	Gln	Lys	Ser	560	Leu	Ala	Ala	Pro	Met	565	Ile	Leu	Ser	Leu	Gln	570
Asp	Lys	Met	Pro	575	Pro	Lys	Ala	Thr	Val	580	Glu	Ser	Trp	Val	Lys	585
Arg	Glu	Ser	Met	590	Lys	Lys	Ser	Gly	Arg	595	Trp	Trp	Phe	Trp	Arg	600
Ser	Glu	Ala	Pro	605	Thr	Lys	Gln	Leu	Pro	610	Glu	Ser	Lys	Glu	Gly	615
Pro	Ala	Gly	Ala	620	Pro	Ala	Ser	Asp	Leu	625	Pro	Ser	Ser	Ser	Lys	630
Gly	Ser	Gln	Glu	635	Arg	Pro	Ala	Glu	Asn	640	Asp	Ser	Ser	Ser	Asp	645
Thr	Glu	Pro	Leu	650	Leu	Glu	Glu	Ser	Ile	655	Thr	Val	Asp	Pro	Ile	660
Leu	Arg	Leu	Ser	665	His	Gly	Ser	Thr	Thr	670	Ser	Tyr	Lys	Lys	Ser	675
				680	Asp	Gln	Ile	Ala	Lys	685	Leu	Lys	Leu	His	Asp	690

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Gly	Pro	Asn	Asp	Val	Val	Phe	Ser	Ile	Thr	Thr	Gln	Tyr	Gln	Gly	
				695					700					705	
Thr	Cys	Arg	Cys	Ala	Gly	Thr	Ile	Tyr	Leu	Trp	Asn	Trp	Asn	Asp	
				710					715					720	
Lys	Ile	Ile	Ile	Ser	Asp	Ile	Asp	Gly	Thr	Ile	Thr	Lys	Ser	Asp	
				725					730					735	
Ala	Leu	Gly	Gln	Ile	Leu	Pro	Gln	Leu	Gly	Lys	Asp	Trp	Thr	His	
				740					745					750	
Gln	Gly	Ile	Ala	Lys	Leu	Tyr	His	Ser	Ile	Asn	Glu	Asn	Gly	Tyr	
				755					760					765	
Lys	Phe	Leu	Tyr	Cys	Ser	Ala	Arg	Ala	Ile	Gly	Met	Ala	Asp	Met	
				770					775					780	
Thr	Arg	Gly	Tyr	Leu	His	Trp	Val	Asn	Asp	Lys	Gly	Thr	Ile	Leu	
				785					790					795	
Pro	Arg	Gly	Pro	Leu	Met	Leu	Ser	Pro	Ser	Ser	Leu	Phe	Ser	Ala	
				800					805					810	
Phe	His	Arg	Glu	Val	Ile	Glu	Lys	Lys	Pro	Glu	Lys	Phe	Lys	Ile	
				815					820					825	
Glu	Cys	Leu	Asn	Asp	Ile	Lys	Asn	Leu	Phe	Ala	Pro	Ser	Lys	Gln	
				830					835					840	
Pro	Phe	Tyr	Ala	Ala	Phe	Gly	Asn	Arg	Pro	Asn	Asp	Val	Tyr	Ala	
				845					850					855	
Tyr	Thr	Gln	Val	Gly	Val	Pro	Asp	Cys	Arg	Ile	Phe	Thr	Val	Asn	
				860					865					870	
Pro	Lys	Gly	Glu	Leu	Ile	Gln	Glu	Arg	Thr	Lys	Gly	Asn	Lys	Ser	
				875					880					885	
Ser	Tyr	His	Arg	Leu	Ser	Glu	Leu	Val	Glu	His	Val	Phe	Pro	Leu	
				890					895					900	
Leu	Ser	Lys	Glu	Gln	Asn	Ser	Ala	Phe	Pro	Cys	Pro	Glu	Phe	Ser	
				905					910					915	
Ser	Phe	Cys	Tyr	Trp	Arg	Asp	Pro	Ile	Pro	Glu	Val	Asp	Leu	Asp	
				920					925					930	

Asp Leu Ser

<210> 32

<211> 268

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1708229CD1

<400> 32

Met	Leu	Gly	Asp	His	Cys	Ser	Leu	Pro	Glu	Asp	Gln	Ala	Arg	Pro	
1				5					10					15	
Gly	Gln	Ser	Leu	Gln	Ser	Gly	Leu	Cys	Cys	Lys	Met	Val	Leu	Gln	
				20					25					30	
Ala	Val	Ser	Lys	Val	Leu	Arg	Lys	Ser	Lys	Ala	Lys	Pro	Asn	Gly	
				35					40					45	
Lys	Lys	Pro	Ala	Ala	Glu	Glu	Arg	Lys	Ala	Tyr	Leu	Glu	Pro	Glu	
				50					55					60	
His	Thr	Lys	Ala	Arg	Ile	Thr	Asp	Phe	Gln	Phe	Lys	Glu	Leu	Val	
				65					70					75	
Val	Leu	Pro	Arg	Glu	Ile	Asp	Leu	Asn	Glu	Trp	Leu	Ala	Ser	Asn	
				80					85					90	
Thr	Thr	Thr	Phe	Phe	His	His	Ile	Asn	Leu	Gln	Tyr	Ser	Thr	Ile	
				95					100					105	
Ser	Glu	Phe	Cys	Thr	Gly	Glu	Thr	Cys	Gln	Thr	Met	Ala	Val	Cys	
				110					115					120	
Asn	Thr	Gln	Tyr	Tyr	Trp	Tyr	Asp	Glu	Arg	Gly	Lys	Lys	Val	Lys	
				125					130					135	
Cys	Thr	Ala	Pro	Gln	Tyr	Val	Asp	Phe	Val	Met	Ser	Ser	Val	Gln	

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Lys Leu Val Thr	140	Asp Glu Asp Val Phe	145	Pro Thr Lys Tyr Gly	150
Glu Phe Pro Ser	155	Phe Glu Ser Leu Val	160	Arg Lys Ile Cys	165
His Leu Phe His	170	Val Leu Ala His Ile	175	Tyr Trp Ala His Phe	180
Glu Thr Leu Ala	185	Leu Glu Leu His Gly	190	His Leu Asn Thr Leu	195
Val His Phe Ile	200	Leu Phe Ala Arg Glu	205	Phe Asn Leu Leu Asp	210
Lys Glu Thr Ala	215	Ile Met Asp Asp Leu	220	Thr Glu Val Leu Cys	225
Gly Ala Gly Gly	230	Val His Ser Gly Gly	235	Ser Gly Asp Gly Ala	240
Ser Gly Gly Pro	245	Gly Ala Gln Asn His	250	Val Lys Glu Arg	255
	260		265		

<210> 33'

<211> 337

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1806454CD1

<400> 33

Met Leu Leu Gly	Leu	Ala	Ala	Met	Glu	Leu	Lys	Val	Trp	Val	Asp
1	5					10					15
Gly Ile Gln Arg	Val	Val	Cys	Gly	Val	Ser	Glu	Gln	Thr	Thr	Cys
	20					25					30
Gln Glu Val Val	Ile	Ala	Leu	Ala	Gln	Ala	Ile	Gly	Gln	Thr	Gly
	35					40					45
Arg Phe Val Leu	Val	Gln	Arg	Leu	Arg	Glu	Lys	Glu	Arg	Gln	Leu
	50					55					60
Leu Pro Gln Glu	Cys	Pro	Val	Gly	Ala	Gln	Ala	Thr	Cys	Gly	Gln
	65					70					75
Phe Ala Ser Asp	Val	Gln	Phe	Val	Leu	Arg	Arg	Thr	Gly	Pro	Ser
	80					85					90
Leu Ala Gly Arg	Pro	Ser	Ser	Asp	Ser	Cys	Pro	Pro	Pro	Glu	Arg
	95					100					105
Cys Leu Ile Arg	Ala	Ser	Leu	Pro	Val	Lys	Pro	Arg	Ala	Ala	Leu
	110					115					120
Gly Cys Glu Pro	Arg	Lys	Thr	Leu	Thr	Pro	Glu	Pro	Ala	Pro	Ser
	125					130					135
Leu Ser Arg Pro	Gly	Pro	Ala	Ala	Pro	Val	Thr	Pro	Thr	Pro	Gly
	140					145					150
Cys Cys Thr Asp	Leu	Arg	Gly	Leu	Glu	Leu	Arg	Val	Gln	Arg	Asn
	155					160					165
Ala Glu Glu Leu	Gly	His	Glu	Ala	Phe	Trp	Glu	Gln	Glu	Leu	Arg
	170					175					180
Arg Glu Gln Ala	Arg	Glu	Arg	Glu	Gly	Gln	Ala	Arg	Leu	Gln	Ala
	185					190					195
Leu Ser Ala Ala	Thr	Ala	Glu	His	Ala	Ala	Arg	Leu	Gln	Ala	Leu
	200					205					210
Asp Ala Gln Ala	Arg	Ala	Leu	Glu	Ala	Glu	Leu	Gln	Leu	Ala	Ala
	215					220					225
Glu Ala Pro Gly	Pro	Pro	Ser	Pro	Met	Ala	Ser	Ala	Thr	Glu	Arg
	230					235					240
Leu His Gln Asp	Leu	Ala	Val	Gln	Glu	Arg	Gln	Ser	Ala	Glu	Val
	245					250					255
Gln Gly Ser Leu	Ala	Leu	Val	Ser	Arg	Ala	Leu	Glu	Ala	Ala	Glu
	260					265					270

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Arg	Ala	Leu	Gln	Ala	Gln	Ala	Gln	Glu	Leu	Glu	Glu	Leu	Asn	Arg	
									275						285
Glu	Leu	Arg	Gln	Cys	Asn	Leu	Gln	Gln	Phe	Ile	Gln	Gln	Thr	Gly	
									290						300
Ala	Ala	Leu	Pro	Pro	Pro	Pro	Arg	Pro	Asp	Arg	Gly	Pro	Pro	Gly	
									305						315
Thr	Gln	Val	Gly	Val	Val	Leu	Gly	Gly	Gly	Trp	Glu	Val	Arg	Thr	
									320						330
Trp	Pro	Ser	Pro	Thr	Pro	Ser			325						
									335						

<210> 34

<211> 565

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1806850CD1

<400> 34

Met	Lys	Glu	Glu	Glu	Glu	Val	Phe	Gln	Pro	Met	Leu	Met	Glu	Tyr	
									1						15
Phe	Thr	Tyr	Glu	Glu	Leu	Lys	Tyr	Ile	Lys	Lys	Lys	Val	Ile	Ala	
									20						30
Gln	His	Cys	Ser	Gln	Lys	Asp	Thr	Ala	Glu	Leu	Leu	Arg	Gly	Leu	
									35						45
Ser	Leu	Trp	Asn	His	Ala	Glu	Glu	Arg	Gln	Lys	Phe	Phe	Lys	Tyr	
									50						60
Ser	Val	Asp	Glu	Lys	Ser	Asp	Lys	Glu	Ala	Glu	Val	Ser	Glu	His	
									65						75
Ser	Thr	Gly	Ile	Thr	His	Leu	Pro	Pro	Glu	Val	Met	Leu	Ser	Ile	
									80						90
Phe	Ser	Tyr	Leu	Asn	Pro	Gln	Glu	Leu	Cys	Arg	Cys	Ser	Gln	Val	
									95						105
Ser	Met	Lys	Trp	Ser	Gln	Leu	Thr	Lys	Thr	Gly	Ser	Leu	Trp	Lys	
									110						120
His	Leu	Tyr	Pro	Val	His	Trp	Ala	Arg	Gly	Asp	Trp	Tyr	Ser	Gly	
									125						135
Pro	Ala	Thr	Glu	Leu	Asp	Thr	Glu	Pro	Asp	Asp	Glu	Trp	Val	Lys	
									140						150
Asn	Arg	Lys	Asp	Glu	Ser	Arg	Ala	Phe	His	Glu	Trp	Asp	Glu	Asp	
									155						165
Ala	Asp	Ile	Asp	Glu	Ser	Glu	Glu	Ser	Ala	Glu	Glu	Ser	Ile	Ala	
									170						180
Ile	Ser	Ile	Ala	Gln	Met	Glu	Lys	Arg	Leu	Leu	His	Gly	Leu	Ile	
									185						195
His	Asn	Val	Leu	Pro	Tyr	Val	Gly	Thr	Ser	Val	Lys	Thr	Leu	Val	
									200						210
Leu	Ala	Tyr	Ser	Ser	Ala	Val	Ser	Ser	Lys	Met	Val	Arg	Gln	Ile	
									215						225
Leu	Glu	Leu	Cys	Pro	Asn	Leu	Glu	His	Leu	Asp	Leu	Thr	Gln	Thr	
									230						240
Asp	Ile	Ser	Asp	Ser	Ala	Phe	Asp	Ser	Trp	Ser	Trp	Leu	Gly	Cys	
									245						255
Cys	Gln	Ser	Leu	Arg	His	Leu	Asp	Leu	Ser	Gly	Cys	Glu	Lys	Ile	
									260						270
Thr	Asp	Val	Ala	Leu	Glu	Lys	Ile	Ser	Arg	Ala	Leu	Gly	Ile	Leu	
									275						285
Thr	Ser	His	Gln	Ser	Gly	Phe	Leu	Lys	Thr	Ser	Thr	Ser	Lys	Ile	
									290						300
Thr	Ser	Thr	Ala	Trp	Lys	Asn	Lys	Asp	Ile	Thr	Met	Gln	Ser	Thr	
									305						315
Lys	Gln	Tyr	Ala	Cys	Leu	His	Asp	Leu	Thr	Asn	Lys	Gly	Ile	Gly	
									310						

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Glu	Glu	Ile	Asp	320	Asn	Glu	His	Pro	Trp	325	Thr	Lys	Pro	Val	Ser	330
				335						340						345
Glu	Asn	Phe	Thr	Ser	350	Pro	Tyr	Val	Trp	355	Met	Leu	Asp	Ala	Glu	360
Leu	Ala	Asp	Ile	Glu	365	Asp	Thr	Val	Glu	370	Trp	Arg	His	Arg	Asn	375
Glu	Ser	Leu	Cys	Val	380	Met	Glu	Thr	Ala	385	Ser	Asn	Phe	Ser	Cys	390
Thr	Ser	Gly	Cys	Phe	395	Ser	Lys	Asp	Ile	400	Val	Gly	Leu	Arg	Thr	405
Val	Cys	Trp	Gln	Gln	410	His	Cys	Ala	Ser	415	Pro	Ala	Phe	Ala	Tyr	420
Gly	His	Ser	Phe	Cys	425	Cys	Thr	Gly	Thr	430	Ala	Leu	Arg	Thr	Met	435
Ser	Leu	Pro	Glu	Ser	440	Ser	Ala	Met	Cys	445	Arg	Lys	Ala	Ala	Arg	450
Arg	Leu	Pro	Arg	Gly	455	Lys	Asp	Leu	Ile	460	Tyr	Phe	Gly	Ser	Glu	465
Ser	Asp	Gln	Glu	Thr	470	Gly	Arg	Val	Leu	475	Leu	Phe	Leu	Ser	Leu	480
Gly	Cys	Tyr	Gln	Ile	485	Thr	Asp	His	Gly	490	Leu	Arg	Val	Leu	Thr	495
Gly	Gly	Gly	Leu	Pro	500	Tyr	Leu	Glu	His	505	Leu	Asn	Leu	Ser	Gly	510
Leu	Thr	Ile	Thr	Gly	515	Ala	Gly	Leu	Gln	520	Asp	Leu	Val	Ser	Ala	525
Pro	Ser	Leu	Asn	Asp	530	Glu	Tyr	Phe	Tyr	535	Tyr	Cys	Asp	Asn	Ile	540
Gly	Pro	His	Ala	Asp	545	Thr	Ala	Ser	Gly	550	Cys	Gln	Asn	Leu	Gln	555
Gly	Phe	Arg	Ala	Cys	560	Cys	Arg	Ser	Gly	565	Glu					

<210> 35

<211> 228

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1851534CD1

<400> 35

Met	Asp	Phe	Ser	Phe	Ser	Phe	Met	Gln	Gly	Ile	Met	Gly	Asn	Thr		
1				5					10					15		
Ile	Gln	Gln	Pro	Pro	Gln	Leu	Ile	Asp	Ser	Ala	Asn	Ile	Arg	Gln		
				20					25					30		
Glu	Asp	Ala	Phe	Asp	Asn	Asn	Ser	Asp	Ile	Ala	Glu	Asp	Gly	Gly		
				35					40					45		
Gln	Thr	Pro	Tyr	Glu	Ala	Thr	Leu	Gln	Gln	Gly	Phe	Gln	Tyr	Pro		
				50					55					60		
Ala	Thr	Thr	Glu	Asp	Leu	Pro	Pro	Leu	Thr	Asn	Gly	Tyr	Pro	Ser		
				65					70					75		
Ser	Ile	Ser	Val	Tyr	Glu	Thr	Gln	Thr	Lys	Tyr	Gln	Ser	Tyr	Asn		
				80					85					90		
Gln	Tyr	Pro	Asn	Gly	Ser	Ala	Asn	Gly	Phe	Gly	Ala	Val	Arg	Asn		
				95					100					105		
Phe	Ser	Pro	Thr	Asp	Tyr	Tyr	His	Ser	Glu	Ile	Pro	Asn	Thr	Arg		
				110					115					120		
Pro	His	Glu	Ile	Leu	Glu	Lys	Pro	Ser	Pro	Pro	Gln	Pro	Pro	Pro		
				125					130					135		
Pro	Pro	Ser	Val	Pro	Gln	Thr	Val	Ile	Pro	Lys	Lys	Thr	Gly	Ser		
				140					145					150		

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Pro Glu Ile Lys Leu Lys Ile Thr Lys Thr Ile Gln Asn Gly Arg
155 160 165
Glu Leu Phe Glu Ser Ser Leu Cys Gly Asp Leu Leu Asn Glu Val
170 175 180
Gln Ala Ser Glu His Thr Lys Ser Lys His Glu Ser Arg Lys Glu
185 190 195
Lys Arg Lys Lys Ser Asn Lys His Asp Ser Ser Arg Ser Glu Glu
200 205 210
Arg Lys Ser His Lys Ile Pro Lys Leu Glu Pro Glu Glu Gln Asn
215 220 225
Met Thr Lys

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<210> 36

<211> 495

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1868749CD1

<400> 36

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Met Lys Gly Met Lys Val Glu Val Leu Asn Ser Asp Ala Val Leu
1 5 10 15
Pro Ser Arg Val Tyr Trp Ile Ala Ser Val Ile Gln Thr Ala Gly
20 25 30
Tyr Arg Val Leu Leu Arg Tyr Glu Gly Phe Glu Asn Asp Ala Ser
35 40 45
His Asp Phe Trp Cys Asn Leu Gly Thr Val Asp Val His Pro Ile
50 55 60
Gly Trp Cys Ala Ile Asn Ser Lys Ile Leu Val Pro Pro Arg Thr
65 70 75
Ile His Ala Lys Phe Thr Asp Trp Lys Gly Tyr Leu Met Lys Arg
80 85 90
Leu Val Gly Ser Arg Thr Leu Pro Val Asp Phe His Ile Lys Met
95 100 105
Val Glu Ser Met Lys Tyr Pro Phe Arg Gln Gly Met Arg Leu Glu
110 115 120
Val Val Asp Lys Ser Gln Val Ser Arg Thr Arg Met Ala Val Val
125 130 135
Asp Thr Val Ile Gly Gly Arg Leu Arg Leu Leu Tyr Glu Asp Gly
140 145 150
Asp Ser Asp Asp Asp Phe Trp Cys His Met Trp Ser Pro Leu Ile
155 160 165
His Pro Val Gly Trp Ser Arg Arg Val Gly His Gly Ile Lys Met
170 175 180
Ser Glu Arg Arg Ser Asp Met Ala His His Pro Thr Phe Arg Lys
185 190 195
Ile Tyr Cys Asp Ala Val Pro Tyr Leu Phe Lys Lys Val Arg Ala
200 205 210
Val Tyr Thr Glu Gly Gly Trp Phe Glu Glu Gly Met Lys Leu Glu
215 220 225
Ala Ile Asp Pro Leu Asn Leu Gly Asn Ile Cys Val Ala Thr Val
230 235 240
Cys Lys Val Leu Leu Asp Gly Tyr Leu Met Ile Cys Val Asp Gly
245 250 255
Gly Pro Ser Thr Asp Gly Leu Asp Trp Phe Cys Tyr His Ala Ser
260 265 270
Ser His Ala Ile Phe Pro Ala Thr Phe Cys Gln Lys Asn Asp Ile
275 280 285
Glu Leu Thr Pro Pro Lys Gly Tyr Glu Ala Gln Thr Phe Asn Trp
290 295 300
Glu Asn Tyr Leu Glu Lys Thr Lys Ser Lys Ala Ala Pro Ser Arg

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Leu Phe Asn Met	305	Asp Cys Pro Asn His	310	Gly Phe Lys Val Gly	315
	320		325		330
Lys Leu Glu Ala	335	Val Asp Leu Met Glu	340	Pro Arg Leu Ile Cys	345
	350	Ala Thr Val Lys Arg	355	Val Val His Arg Leu	360
Ala Thr Val Lys	365	Val Val His Arg	370	Leu Ser Ile His	375
Asp Gly Trp Asp	380	Ser Glu Tyr Asp Gln	385	Trp Val Asp Cys Glu	390
	395	Pro Asp Ile Tyr Pro	400	Val Gly Trp Cys Glu	405
Pro Asp Ile Tyr	410	Val Val Ala Ala Glu	415	Leu Thr Gly Tyr Gln	420
	425	Leu Gln Pro Pro Val	430	Ala Thr Pro Leu Lys	435
Lys Glu Ala Thr	440	Lys Lys Lys Lys Lys	445	Gln Phe Gly Lys Lys	450
	455	Lys Arg Ile Pro Pro	460	Thr Lys Lys Lys Arg	465
Lys Arg Ile Pro	470	Thr Lys Thr Arg Pro	475	Leu Arg Gln Gly Ser	480
	485	Lys Lys Pro Leu Leu	490	Gln Gly Ala Arg Lys	495
Lys Lys Pro Leu		Glu Asp Asp Pro Gln		Ala Arg Lys Ile	
Ser Ser Glu Pro		Val Pro Gly Glu Ile		Ile Ala Val Arg Val	
		Glu Glu His Leu Asp		Lys Ala Ser Ser Pro	
Glu Glu His Leu		Val Ala Ser Pro Asp		Lys Ala Ser Ser Pro	
Glu Leu Pro Val		Ser Val Glu Asn Ile		Lys Gln Glu Thr Asp	

<210> 37

<211> 1336

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1980010CD1

<400> 37

Met Val Asp Gln	Leu	Glu	Gln	Ile	Leu	Ser	Val	Ser	Glu	Leu	Leu
1	5					10					15
Glu Lys His Gly	Leu	Glu	Lys	Pro	Ile	Ser	Phe	Val	Lys	Asn	Thr
	20					25					30
Gln Ser Ser Ser	Glu	Glu	Ala	Arg	Lys	Leu	Met	Val	Arg	Leu	Thr
	35					40					45
Arg His Thr Gly	Arg	Lys	Gln	Pro	Pro	Val	Ser	Glu	Ser	His	Trp
	50					55					60
Arg Thr Leu Leu	Gln	Asp	Met	Leu	Thr	Met	Gln	Gln	Asn	Val	Tyr
	65					70					75
Thr Cys Leu Asp	Ser	Asp	Ala	Cys	Tyr	Glu	Ile	Phe	Thr	Glu	Ser
	80					85					90
Leu Leu Cys Ser	Ser	Arg	Leu	Glu	Asn	Ile	His	Leu	Ala	Gly	Gln
	95					100					105
Met Met His Cys	Ser	Ala	Cys	Ser	Glu	Asn	Pro	Pro	Ala	Gly	Ile
	110					115					120
Ala His Lys Gly	Asn	Pro	His	Tyr	Arg	Val	Ser	Tyr	Glu	Lys	Ser
	125					130					135
Ile Asp Leu Val	Leu	Ala	Ala	Ser	Arg	Glu	Tyr	Phe	Asn	Ser	Ser
	140					145					150
Thr Asn Leu Thr	Asp	Ser	Cys	Met	Asp	Leu	Ala	Arg	Cys	Cys	Leu
	155					160					165
Gln Leu Ile Thr	Asp	Arg	Pro	Pro	Ala	Ile	Gln	Glu	Glu	Leu	Asp
	170					175					180
Leu Ile Gln Ala	Val	Gly	Cys	Leu	Glu	Glu	Phe	Gly	Val	Lys	Ile
	185					190					195
Leu Pro Leu Gln	Val	Arg	Leu	Cys	Pro	Asp	Arg	Ile	Ser	Leu	Ile

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Lys Glu Cys Ile	200	Gln Ser Pro Thr	205	Tyr Lys Gln Ser	210
	215		220		225
Lys Leu Leu Gly	230	Leu Ala Glu Leu Leu	235	Arg Val Ala Gly Glu	240
	245		250		255
Pro Glu Glu Arg	260	Arg Gly Gln Val Leu	265	Ile Leu Leu Val Glu	270
	275		280		285
Ala Leu Arg Phe	290	His Asp Tyr Lys Ala	295	Ala Ser Met His Cys	300
	305		310		315
Glu Leu Met Ala	320	Thr Gly Tyr Pro Lys	325	Ser Trp Asp Val Cys	330
	335		340		345
Gln Leu Gly Gln	350	Ser Glu Gly Tyr Gln	355	Asp Leu Ala Thr Arg	360
	365		370		375
Glu Leu Met Ala	380	Phe Ala Leu Thr His	385	Cys Pro Pro Ser Ser	390
	395		400		405
Glu Leu Leu Leu	410	Ala Ala Ser Ser Ser	415	Leu Gln Thr Glu Ile	420
	425		430		435
Tyr Gln Arg Val	440	Asn Phe Gln Ile His	445	His Glu Gly Gly Glu	450
	455		460		465
Ile Ser Ala Ser	470	Pro Leu Thr Ser Lys	475	Ala Val Gln Glu Asp	480
	485		490		495
Val Gly Val Pro	500	Gly Ser Asn Ser Ala	505	Asp Leu Leu Arg Trp	510
	515		520		525
Thr Ala Thr Thr	530	Met Lys Val Leu Ser	535	Asn Thr Thr Thr Thr	540
	545		550		555
Lys Ala Val Leu	560	Gln Ala Val Ser Asp	565	Gly Gln Trp Trp Lys	570
	575		580		585
Ser Leu Thr Tyr	590	Leu Arg Pro Leu Gln	595	Gly Gln Lys Cys Gly	600
	605		610		615
Ala Tyr Gln Ile	620	Gly Thr Thr Ala Asn	625	Glu Asp Leu Glu Lys	630
	635		640		645
Gly Cys His Pro	650	Phe Tyr Glu Ser Val	655	Ile Ser Asn Pro Phe	660
	665		670		675
Ala Glu Ser Glu	680	Gly Thr Tyr Asp Thr	685	Tyr Gln His Val Pro	690
	695		700		705
Glu Ser Phe Ala	710	Glu Val Leu Leu Arg	715	Thr Gly Lys Leu Ala	720
	725		730		735
Ala Lys Asn Lys	740	Gly Glu Val Phe Pro	745	Thr Thr Glu Val Leu	750
	755		760		765
Gln Leu Ala Ser	770	Glu Ala Leu Pro Asn	775	Asp Met Thr Leu Ala	780
	785		790		795
Ala Tyr Leu Leu	800	Ala Leu Pro Gln Val	805	Leu Asp Ala Asn Arg	810
	815		820		825
Phe Glu Lys Gln	830	Ser Pro Ser Ala Leu	835	Ser Leu Gln Leu Ala	840
	845		850		855
Tyr Tyr Tyr Ser	860	Leu Gln Ile Tyr Ala	865	Arg Leu Ala Pro Cys	870
	875		880		885
Arg Asp Lys Cys	890	His Pro Leu Tyr Arg	895	Ala Asp Pro Lys Glu	900
	905		910		915
Ile Lys Met Val	920	Thr Arg His Val Thr	925	Arg His Glu His Glu	930
	935		940		945
Trp Pro Glu Asp	950	Leu Ile Ser Leu Thr	955	Lys Gln Leu His Cys	960
	965		970		975
Asn Glu Arg Leu	980	Leu Asp Phe Thr Gln	985	Ala Gln Ile Leu Gln	990
	995		1000		1005
Leu Arg Lys Gly	1010	Val Asp Val Gln Arg	1015	Phe Thr Ala Asp Asp	1020
	1025		1030		1035
Tyr Lys Arg Glu	1040	Thr Ile Leu Gly Leu	1045	Ala Glu Thr Leu Glu	1050
	1055		1060		1065
Ser Val Tyr Ser	1070	Ile Ala Ile Ser Leu	1075	Ala Gln Arg Tyr Ser	1080
	1085		1090		1095
Ser Arg Trp Glu	1100	Val Phe Met Thr His	1105	Leu Glu Phe Leu Phe	1110
	1115		1120		1125

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Asp	Ser	Gly	Leu	Ser	Thr	Leu	Glu	Ile	Glu	Asn	Arg	Ala	Gln	Asp	680
Leu	His	Leu	Phe	Glu	Thr	Leu	Lys	Thr	Asp	Pro	Glu	Ala	Phe	His	690
Gln	His	Met	Val	Lys	Tyr	Ile	Tyr	Pro	Thr	Ile	Gly	Gly	Phe	Asp	700
His	Glu	Arg	Leu	Gln	Tyr	Tyr	Phe	Thr	Leu	Leu	Glu	Asn	Cys	Gly	710
Cys	Ala	Asp	Leu	Gly	Asn	Cys	Ala	Ile	Lys	Pro	Glu	Thr	His	Ile	720
Arg	Leu	Leu	Lys	Lys	Phe	Lys	Val	Val	Ala	Ser	Gly	Leu	Asn	Tyr	730
Lys	Lys	Leu	Thr	Asp	Glu	Asn	Met	Ser	Pro	Leu	Glu	Ala	Leu	Glu	740
Pro	Val	Leu	Ser	Ser	Gln	Asn	Ile	Leu	Ser	Ile	Ser	Lys	Leu	Val	750
Pro	Lys	Ile	Pro	Glu	Lys	Asp	Gly	Gln	Met	Leu	Ser	Pro	Ser	Ser	760
Leu	Tyr	Thr	Ile	Trp	Leu	Gln	Lys	Leu	Phe	Trp	Thr	Gly	Asp	Pro	770
His	Leu	Ile	Lys	Gln	Val	Pro	Gly	Ser	Ser	Pro	Glu	Trp	Leu	His	780
Ala	Tyr	Asp	Val	Cys	Met	Lys	Tyr	Phe	Asp	Arg	Leu	His	Pro	Gly	790
Asp	Leu	Ile	Thr	Val	Val	Asp	Ala	Val	Thr	Phe	Ser	Pro	Lys	Ala	800
Val	Thr	Lys	Leu	Ser	Val	Glu	Ala	Arg	Lys	Glu	Met	Thr	Arg	Lys	810
Ala	Ile	Lys	Thr	Val	Lys	His	Phe	Ile	Glu	Lys	Pro	Arg	Lys	Arg	820
Asn	Ser	Glu	Asp	Glu	Ala	Gln	Glu	Ala	Lys	Asp	Ser	Lys	Val	Thr	830
Tyr	Ala	Asp	Thr	Leu	Asn	His	Leu	Glu	Lys	Ser	Leu	Ala	His	Leu	840
Glu	Thr	Leu	Ser	His	Ser	Phe	Ile	Leu	Ser	Leu	Lys	Asn	Ser	Glu	850
Gln	Glu	Thr	Leu	Gln	Lys	Tyr	Ser	His	Leu	Tyr	Asp	Leu	Ser	Arg	860
Ser	Glu	Lys	Glu	Lys	Leu	His	Asp	Glu	Ala	Val	Ala	Ile	Cys	Leu	870
Asp	Gly	Gln	Pro	Leu	Ala	Met	Ile	Gln	Gln	Leu	Leu	Glu	Val	Ala	880
Val	Gly	Pro	Leu	Asp	Ile	Ser	Pro	Lys	Asp	Ile	Val	Gln	Ser	Ala	890
Ile	Met	Lys	Ile	Ile	Ser	Ala	Leu	Ser	Gly	Gly	Ser	Ala	Asp	Leu	900
Gly	Gly	Pro	Arg	Asp	Pro	Leu	Lys	Val	Leu	Glu	Gly	Val	Val	Ala	910
Ala	Val	His	Ala	Ser	Val	Asp	Lys	Gly	Glu	Glu	Leu	Val	Ser	Pro	920
Glu	Asp	Leu	Leu	Glu	Trp	Leu	Arg	Pro	Phe	Cys	Ala	Asp	Asp	Ala	930
Trp	Pro	Val	Arg	Pro	Arg	Ile	His	Val	Leu	Gln	Ile	Leu	Gly	Gln	940
Ser	Phe	His	Leu	Thr	Glu	Glu	Asp	Ser	Lys	Leu	Leu	Val	Phe	Phe	950
Arg	Thr	Glu	Ala	Ile	Leu	Lys	Ala	Ser	Trp	Pro	Gln	Arg	Gln	Val	960
Asp	Ile	Ala	Asp	Ile	Glu	Asn	Glu	Glu	Asn	Arg	Tyr	Cys	Leu	Phe	970
Met	Glu	Leu	Leu	Glu	Ser	Ser	His	His	Glu	Ala	Glu	Phe	Gln	His	980
Leu	Val	Leu	Leu	Leu	Gln	Ala	Trp	Pro	Pro	Met	Lys	Ser	Glu	Tyr	990

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Val Ile Thr Asn Asn Pro Trp Val Arg Leu Ala Thr Val Met Leu	1145	1150	1155
	1160	1165	1170
Thr Arg Cys Thr Met Glu Asn Lys Glu Gly Leu Gly Asn Glu Val	1175	1180	1185
Leu Lys Met Cys Arg Ser Leu Tyr Asn Thr Lys Gln Met Leu Pro	1190	1195	1200
Ala Glu Gly Val Lys Glu Leu Cys Leu Leu Asn Gln Ser	1205	1210	1215
Leu Leu Leu Pro Ser Leu Lys Leu Leu Leu Glu Ser Arg Asp Glu	1220	1225	1230
His Leu His Glu Met Ala Leu Glu Gln Ile Thr Ala Val Thr Thr	1235	1240	1245
Val Asn Asp Ser Asn Cys Asp Gln Glu Leu Leu Ser Leu Leu Leu	1250	1255	1260
Asp Ala Lys Leu Leu Val Lys Cys Val Ser Thr Pro Phe Tyr Pro	1265	1270	1275
Arg Ile Val Asp His Leu Leu Ala Ser Leu Gln Gln Gly Arg Trp	1280	1285	1290
Asp Ala Glu Glu Leu Gly Arg His Leu Arg Glu Ala Gly His Glu	1295	1300	1305
Ala Glu Ala Gly Ser Leu Leu Leu Ala Val Arg Gly Thr His Gln	1310	1315	1320
Ala Phe Arg Thr Phe Ser Thr Ala Leu Arg Ala Ala Gln His Trp	1325	1330	1335
Val			

<210> 38

<211> 934

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2259032CD1

<400> 38

Met Phe Trp Lys Phe Asp Leu Asn Thr Thr Ser His Val Asp Lys	1	5	10	15
Leu Leu Asp Lys Glu His Val Thr Leu Gln Glu Leu Met Asp Glu	20	25	30	35
Asp Asp Ile Leu Gln Glu Cys Lys Ala Gln Asn Gln Lys Leu Leu	40	45	50	55
Asp Phe Leu Cys Arg Gln Gln Cys Met Glu Glu Leu Val Ser Leu	60	65	70	75
Ile Thr Gln Asp Pro Pro Leu Asp Met Glu Glu Lys Val Arg Phe	80	85	90	95
Lys Tyr Pro Asn Thr Ala Cys Glu Leu Leu Thr Cys Asp Val Pro	100	105	110	115
Gln Ile Ser Asp Arg Leu Gly Gly Asp Glu Ser Leu Leu Ser Leu	120	125	130	135
Leu Tyr Asp Phe Leu Asp His Glu Pro Pro Leu Asn Pro Leu Leu	140	145	150	155
Ala Ser Phe Phe Ser Lys Thr Ile Gly Asn Leu Ile Ala Arg Lys	160	165	170	175
Thr Glu Gln Val Ile Thr Phe Leu Lys Lys Asp Lys Phe Ile	180	185	190	
Ser Leu Val Leu Lys His Ile Gly Thr Ser Ala Leu Met Asp Leu				
Leu Leu Arg Leu Val Ser Cys Val Glu Pro Ala Gly Leu Arg Gln				
Asp Val Leu His Trp Leu Asn Glu Glu Lys Val Ile Gln Arg Leu				

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Val	Glu	Leu	Ile	His	Pro	Ser	Gln	Asp	Glu	Asp	Arg	Gln	Ser	Asn
				200					205					210
Ala	Ser	Gln	Thr	Leu	Cys	Asp	Ile	Val	Arg	Leu	Gly	Arg	Asp	Gln
				215					220					225
Gly	Ser	Gln	Leu	Gln	Glu	Ala	Leu	Glu	Pro	Asp	Pro	Leu	Leu	Thr
				230					235					240
Ala	Leu	Glu	Ser	Arg	Gln	Asp	Cys	Val	Glu	Gln	Leu	Leu	Lys	Asn
				245					250					255
Met	Phe	Asp	Gly	Asp	Arg	Thr	Glu	Ser	Cys	Leu	Val	Ser	Gly	Thr
				260					265					270
Gln	Val	Leu	Leu	Thr	Leu	Leu	Glu	Thr	Arg	Arg	Val	Gly	Thr	Glu
				275					280					285
Gly	Leu	Val	Asp	Ser	Phe	Ser	Gln	Gly	Leu	Glu	Arg	Ser	Tyr	Ala
				290					295					300
Val	Ser	Ser	Ser	Val	Leu	His	Gly	Ile	Glu	Pro	Arg	Leu	Lys	Asp
				305					310					315
Phe	His	Gln	Leu	Leu	Leu	Asn	Pro	Pro	Lys	Lys	Lys	Ala	Ile	Leu
				320					325					330
Thr	Thr	Ile	Gly	Val	Leu	Glu	Glu	Pro	Leu	Gly	Asn	Ala	Arg	Leu
				335					340					345
His	Gly	Ala	Arg	Leu	Met	Ala	Ala	Leu	Leu	His	Thr	Asn	Thr	Pro
				350					355					360
Ser	Ile	Asn	Gln	Glu	Leu	Cys	Arg	Leu	Asn	Thr	Met	Asp	Leu	Leu
				365					370					375
Leu	Asp	Leu	Phe	Phe	Lys	Tyr	Thr	Trp	Asn	Asn	Phe	Leu	His	Phe
				380					385					390
Gln	Val	Glu	Leu	Cys	Ile	Ala	Ala	Ile	Leu	Ser	His	Ala	Ala	Arg
				395					400					405
Glu	Glu	Arg	Thr	Glu	Ala	Ser	Gly	Ser	Glu	Ser	Arg	Val	Glu	Pro
				410					415					420
Pro	His	Glu	Asn	Gly	Asn	Arg	Ser	Leu	Glu	Thr	Pro	Gln	Pro	Ala
				425					430					435
Ala	Ser	Leu	Pro	Asp	Asn	Thr	Met	Val	Thr	His	Leu	Phe	Gln	Lys
				440					445					450
Cys	Cys	Leu	Val	Gln	Arg	Ile	Leu	Glu	Ala	Trp	Glu	Ala	Asn	Asp
				455					460					465
His	Thr	Gln	Ala	Ala	Gly	Gly	Met	Arg	Arg	Gly	Asn	Met	Gly	His
				470					475					480
Leu	Thr	Arg	Ile	Ala	Asn	Ala	Val	Val	Gln	Asn	Leu	Glu	Arg	Gly
				485					490					495
Pro	Val	Gln	Thr	His	Ile	Ser	Glu	Val	Ile	Arg	Gly	Leu	Pro	Ala
				500					505					510
Asp	Cys	Arg	Gly	Arg	Trp	Glu	Ser	Phe	Val	Glu	Glu	Thr	Leu	Thr
				515					520					525
Glu	Thr	Asn	Arg	Arg	Asn	Thr	Val	Asp	Leu	Ala	Phe	Ser	Asp	Tyr
				530					535					540
Gln	Ile	Gln	Gln	Met	Thr	Ala	Asn	Phe	Val	Asp	Gln	Phe	Gly	Phe
				545					550					555
Asn	Asp	Glu	Glu	Phe	Ala	Asp	Gln	Asp	Asp	Asn	Ile	Asn	Ala	Pro
				560					565					570
Phe	Asp	Arg	Ile	Ala	Glu	Ile	Asn	Phe	Asn	Ile	Asp	Ala	Asp	Glu
				575					580					585
Asp	Ser	Pro	Ser	Ala	Ala	Leu	Phe	Glu	Ala	Cys	Cys	Ser	Asp	Arg
				590					595					600
Ile	Gln	Pro	Phe	Asp	Asp	Asp	Glu	Asp	Glu	Asp	Ile	Trp	Glu	Asp
				605					610					615
Ser	Asp	Thr	Arg	Cys	Ala	Ala	Arg	Val	Met	Ala	Arg	Pro	Arg	Phe
				620					625					630
Gly	Ala	Pro	His	Ala	Ser	Glu	Ser	Cys	Ser	Lys	Asn	Gly	Pro	Glu
				635					640					645
Arg	Gly	Gly	Gln	Asp	Gly	Lys	Ala	Ser	Leu	Glu	Ala	His	Arg	Asp
				650					655					660
Ala	Pro	Gly	Ala	Gly	Ala	Pro	Pro	Ala	Pro	Gly	Lys	Lys	Glu	Ala

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Pro	Pro	Val	Glu	665	Gly	Asp	Ser	Glu	Ala	670	Gly	Ala	Met	Trp	Thr	675
				680						685						690
Val	Phe	Asp	Glu	695	Pro	Ala	Asn	Ser	Thr	700	Pro	Thr	Ala	Pro	Gly	705
				710						715						720
Val	Arg	Asp	Val	725	Gly	Ser	Ser	Val	Trp	730	Ala	Ala	Gly	Thr	Ser	735
				740						745						750
Pro	Glu	Glu	Lys	755	Gly	Trp	Ala	Lys	Phe	760	Thr	Asp	Phe	Gln	Pro	765
				770						775						780
Cys	Cys	Ser	Glu	785	Ser	Gly	Pro	Arg	Cys	790	Ser	Ser	Pro	Val	Asp	795
				800						805						810
Glu	Cys	Ser	His	815	Ala	Glu	Gly	Ser	Arg	820	Ser	Gln	Gly	Pro	Glu	825
				830						835						840
Ala	Phe	Ser	Pro	845	Ala	Ser	Pro	Cys	Ala	850	Trp	Asn	Val	Cys	Val	855
				860						865						870
Arg	Lys	Ala	Pro	875	Leu	Leu	Ala	Ser	Asp	880	Ser	Ser	Ser	Ser	Gly	885
				880						885						890
Ser	His	Ser	Glu	890	Asp	Gly	Asp	Gln	Lys	905	Ala	Ala	Ser	Ala	Met	910
				905						910						915
Ala	Val	Ser	Arg	920	Gly	Pro	Gly	Arg	Glu	925	Ala	Pro	Pro	Leu	Pro	930
Val	Ala	Arg	Thr		Glu	Glu	Ala	Val	Gly		Arg	Val	Gly	Cys	Ala	
Ser	Arg	Leu	Leu		Pro	Ala	Cys	Pro	Ala		Pro	Lys	Glu	Val	Thr	
Ala	Ala	Pro	Ala		Val	Ala	Val	Pro	Pro		Glu	Ala	Thr	Val	Ala	
Thr	Thr	Ala	Leu		Ser	Lys	Ala	Gly	Pro		Ala	Ile	Pro	Thr	Pro	
Val	Ser	Ser	Ala		Leu	Ala	Val	Ala	Val		Pro	Leu	Gly	Pro	Ile	
Ala	Val	Thr	Ala		Pro	Ala	Met	Val	Ala		Thr	Leu	Gly	Thr	Val	
Thr	Lys	Asp	Gly		Lys	Thr	Asp	Ala	Pro		Pro	Glu	Gly	Ala	Ala	
Asn	Gly	Pro	Val													

<210> 39

<211> 515

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2359526CD1

<400> 39

Met	Ala	Ala	Asn	Met	Tyr	Arg	Val	Gly	Asp	Tyr	Val	Tyr	Phe	Glu	
				5					10					15	
Asn	Ser	Ser	Ser	Asn	Pro	Tyr	Leu	Ile	Arg	Arg	Ile	Glu	Glu	Leu	
				20					25					30	
Asn	Lys	Thr	Ala	Ser	Gly	Asn	Val	Glu	Ala	Lys	Val	Val	Cys	Phe	
				35					40					45	
Tyr	Arg	Arg	Arg	Asp	Ile	Ser	Asn	Thr	Leu	Ile	Met	Leu	Ala	Asp	
				50					55					60	
Lys	His	Ala	Lys	Glu	Ile	Glu	Glu	Glu	Ser	Glu	Thr	Thr	Val	Glu	
				65					70					75	
Ala	Asp	Leu	Thr	Asp	Lys	Gln	Lys	His	Gln	Leu	Lys	His	Arg	Glu	
				80					85					90	
Leu	Phe	Leu	Ser	Arg	Gln	Tyr	Glu	Ser	Leu	Pro	Ala	Thr	His	Ile	
				95					100					105	
Arg	Gly	Lys	Cys	Ser	Val	Ala	Leu	Leu	Asn	Glu	Thr	Glu	Ser	Val	
				110					115					120	

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Leu Ser Tyr Leu Asp Lys Glu Asp Thr Phe Phe Tyr Ser Leu Val
125 130
Tyr Asp Pro Ser Leu Lys Thr Leu Leu Ala Asp Lys Gly Glu Ile
140 145
Arg Val Gly Pro Arg Tyr Gln Ala Asp Ile Pro Glu Met Leu Leu
155 160
Glu Gly Glu Ser Asp Glu Arg Glu Gln Ser Lys Leu Glu Val Lys
170 175
Val Trp Asp Pro Asn Ser Pro Leu Thr Asp Arg Gln Ile Asp Gln
185 190
Phe Leu Val Val Ala Arg Ala Val Gly Thr Phe Ala Arg Ala Leu
200 205
Asp Cys Ser Ser Ser Val Arg Gln Pro Ser Leu His Met Ser Ala
215 220
Ala Ala Ala Ser Arg Asp Ile Thr Leu Phe His Ala Met Asp Thr
230 235
Leu Tyr Arg His Ser Tyr Asp Leu Ser Ser Ala Ile Ser Val Leu
245 250
Val Pro Leu Gly Gly Pro Val Leu Cys Arg Asp Glu Met Glu Glu
260 265
Trp Ser Ala Ser Glu Ala Ser Leu Phe Glu Glu Ala Leu Glu Lys
275 280
Tyr Gly Lys Asp Phe Asn Asp Ile Arg Gln Asp Phe Leu Pro Trp
290 295
Lys Ser Leu Thr Ser Ile Ile Glu Tyr Tyr Tyr Met Trp Lys Thr
305 310
Thr Asp Arg Tyr Val Gln Gln Lys Arg Leu Lys Ala Ala Glu Ala
320 325
Glu Ser Lys Leu Lys Gln Val Tyr Ile Pro Thr Tyr Ser Lys Pro
335 340
Asn Pro Asn Gln Ile Ser Thr Ser Asn Gly Lys Pro Gly Ala Val
350 355
Asn Gly Ala Val Gly Thr Thr Phe Gln Pro Gln Asn Pro Leu Leu
365 370
Gly Arg Ala Cys Glu Ser Cys Tyr Ala Thr Gln Ser His Gln Trp
380 385
Tyr Ser Trp Gly Pro Pro Asn Met Gln Cys Arg Leu Cys Ala Ile
395 400
Cys Trp Leu Tyr Trp Lys Lys Tyr Gly Gly Leu Lys Met Pro Thr
410 415
Gln Ser Glu Glu Glu Lys Leu Ser Pro Ser Pro Thr Thr Glu Asp
425 430
Pro Arg Val Arg Ser His Val Ser Arg Gln Ala Met Gln Gly Met
440 445
Pro Val Arg Asn Thr Gly Ser Pro Lys Ser Ala Val Lys Thr Arg
455 460
Gln Ala Phe Phe Leu His Thr Thr Tyr Phe Thr Lys Phe Ala Arg
470 475
Gln Val Cys Lys Asn Thr Leu Arg Leu Arg Gln Ala Ala Arg Arg
485 490
Pro Phe Val Ala Ile Asn Tyr Ala Ala Ile Arg Ala Glu Cys Lys
500 505
Met Leu Leu Asn Ser 510
515

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<210> 40

<211> 146

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2456494CD1

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<400> 40

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Met Val Asp Glu Leu Val Leu Leu Leu His Ala Leu Leu Met Arg
 1          5          10          15
His Arg Ala Leu Ser Ile Glu Asn Ser Gln Leu Met Glu Gln Leu
 20          25          30
Arg Leu Leu Val Cys Glu Arg Ala Ser Leu Leu Arg Gln Val Arg
 35          40          45
Pro Pro Ser Cys Pro Val Pro Phe Pro Glu Thr Phe Asn Gly Glu
 50          55          60
Ser Ser Arg Leu Pro Glu Phe Ile Val Gln Thr Ala Ser Tyr Met
 65          70          75
Leu Val Asn Glu Asn Arg Phe Cys Asn Asp Ala Met Lys Val Ala
 80          85          90
Phe Leu Ile Ser Leu Leu Thr Gly Glu Ala Glu Glu Trp Val Val
 95          100         105
Pro Tyr Ile Glu Met Asp Ser Pro Ile Leu Gly Asp Tyr Arg Ala
110         115         120
Phe Leu Asp Glu Met Lys Gln Cys Phe Gly Trp Asp Asp Asp Glu
125         130         135
Asp Asp Asp Asp Glu Glu Glu Glu Asp Asp Tyr
140         145

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<210> 41

<211> 580

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2668536CD1

<400> 41

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Met Lys Glu Asn Lys Glu Asn Ser Ser Pro Ser Val Thr Ser Ala
 1          5          10          15
Asn Leu Asp His Thr Lys Pro Cys Trp Tyr Trp Asp Lys Lys Asp
 20          25          30
Leu Ala His Thr Pro Ser Gln Leu Glu Gly Leu Asp Pro Ala Thr
 35          40          45
Glu Ala Arg Tyr Arg Arg Glu Gly Ala Arg Phe Ile Phe Asp Val
 50          55          60
Gly Thr Arg Leu Gly Leu His Tyr Asp Thr Leu Ala Thr Gly Ile
 65          70          75
Ile Tyr Phe His Arg Phe Tyr Met Phe His Ser Phe Lys Gln Phe
 80          85          90
Pro Arg Tyr Val Thr Gly Ala Cys Cys Leu Phe Leu Ala Gly Lys
 95          100         105
Val Glu Glu Thr Pro Lys Lys Cys Lys Asp Ile Ile Lys Thr Ala
110         115         120
Arg Ser Leu Leu Asn Asp Val Gln Phe Gly Gln Phe Gly Asp Asp
125         130         135
Pro Lys Glu Glu Val Met Val Leu Glu Arg Ile Leu Leu Gln Thr
140         145         150
Ile Lys Phe Asp Leu Gln Val Glu His Pro Tyr Gln Phe Leu Leu
155         160         165
Lys Tyr Ala Lys Gln Leu Lys Gly Asp Lys Asn Lys Ile Gln Lys
170         175         180
Leu Val Gln Met Ala Trp Thr Phe Val Asn Asp Ser Leu Cys Thr
185         190         195
Thr Leu Ser Leu Gln Trp Glu Pro Glu Ile Ala Val Ala Val
200         205         210
Met Tyr Leu Ala Gly Arg Leu Cys Lys Phe Glu Ile Gln Glu Trp
215         220         225
Thr Ser Lys Pro Met Tyr Arg Arg Trp Trp Glu Gln Phe Val Gln
230         235

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Asp Val Pro Val Asp Val Leu Glu Asp Ile Cys His Gln Ile Leu
245 250 255
Asp Leu Tyr Ser Gln Gly Lys Gln Gln Met Pro His His Thr Pro
260 265 270
His Gln Leu Gln Gln Pro Pro Ser Leu Gln Pro Thr Pro Gln Val
275 280 285
Pro Gln Val Gln Gln Ser Gln Pro Ser Gln Ser Ser Glu Pro Ser
290 295 300
Gln Pro Gln Gln Lys Asp Pro Gln Gln Pro Ala Gln Gln Gln Gln
305 310 315
Pro Ala Gln Gln Pro Lys Lys Pro Ser Pro Gln Pro Ser Ser Pro
320 325 330
Arg Gln Val Lys Arg Ala Val Val Val Ser Pro Lys Glu Glu Asn
335 340 345
Lys Ala Ala Glu Pro Pro Pro Pro Lys Ile Pro Lys Ile Glu Thr
350 355 360
Thr His Pro Pro Leu Pro Pro Ala His Pro Pro Pro Asp Arg Lys
365 370 375
Pro Pro Leu Ala Ala Ala Leu Gly Glu Ala Glu Pro Pro Gly Pro
380 385 390
Val Asp Ala Thr Asp Leu Pro Lys Val Gln Ile Pro Pro Pro Ala
395 400 405
His Pro Ala Pro Val His Gln Pro Pro Pro Leu Pro His Arg Pro
410 415 420
Pro Pro Pro Pro Pro Ser Ser Tyr Met Thr Gly Met Ser Thr Thr
425 430 435
Ser Ser Tyr Met Ser Gly Glu Gly Tyr Gln Ser Leu Gln Ser Met
440 445 450
Met Lys Thr Glu Gly Pro Ser Tyr Gly Ala Leu Pro Pro Ala Tyr
455 460 465
Gly Pro Pro Ala His Leu Pro Tyr His Pro His Val Tyr Pro Pro
470 475 480
Asn Pro Pro Pro Pro Pro Val Pro Pro Pro Pro Ala Ser Phe Pro
485 490 495
His Leu Pro Ser His Pro Leu Leu Leu Ala Thr Pro Asn Pro His
500 505 510
Pro Pro Thr Thr Pro Thr Ser His Pro His Pro His Ala Ser Arg
515 520 525
Leu Pro Thr Gln Ser Pro Leu Ile Leu Leu Gln Gly Trp Ala Cys
530 535 540
Arg Gln Pro Ala Thr His Leu Leu Pro Ser Pro Leu Glu Asp Ser
545 550 555
Leu Leu Cys Pro Arg Pro Phe Pro His Pro Ala Cys Leu Gln Leu
560 565 570
Glu Gly Leu Gly Arg Ala Ala Trp Met Arg
575 580

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<210> 42

<211> 131

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2683225CD1

<400> 42

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Met Ala Glu Pro Asp Tyr Ile Glu Asp Asp Asn Pro Glu Leu Ile
1 5 10 15
Arg Pro Gln Lys Leu Ile Asn Pro Val Lys Thr Ser Arg Asn His
20 25 30
Gln Asp Leu His Arg Glu Leu Leu Met Asn Gln Lys Arg Gly Leu
35 40 45
Ala Pro Gln Asn Lys Pro Glu Leu Gln Lys Val Met Glu Lys Arg

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Lys Arg Asp Gln Val Ile Lys Gln Lys Glu Glu Ala Gln Lys	50	55	60
	65	70	75
Lys Lys Ser Asp Leu Glu Ile Glu Leu Leu Lys Arg Gln Gln Lys	80	85	90
Leu Glu Gln Leu Glu Leu Glu Lys Gln Lys Leu Gln Glu Glu Gln	95	100	105
Glu Asn Ala Pro Glu Phe Val Lys Val Lys Gly Asn Leu Arg Arg	110	115	120
Thr Gly Gln Glu Val Ala Gln Ala Gln Glu Ser	125	130	

<210> 43

<211> 812

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2797839CD1

<400> 43

Met Gly Arg Lys Leu Asp Pro Thr Lys Glu Lys Arg Gly Pro Gly	1	5	10	15
Arg Lys Ala Arg Lys Gln Lys Gly Ala Glu Thr Glu Leu Val Arg	20	25	30	35
Phe Leu Pro Ala Val Ser Asp Glu Asn Ser Lys Arg Leu Ser Ser	35	40	45	50
Arg Ala Arg Lys Arg Ala Ala Lys Arg Arg Leu Gly Ser Val Glu	50	55	60	65
Ala Pro Lys Thr Asn Lys Ser Pro Glu Ala Lys Pro Leu Pro Gly	65	70	75	80
Lys Leu Pro Lys Gly Ile Ser Ala Gly Ala Val Gln Thr Ala Gly	80	85	90	95
Lys Lys Gly Pro Gln Ser Leu Phe Asn Ala Pro Arg Gly Lys Lys	95	100	105	110
Arg Pro Ala Pro Gly Ser Asp Glu Glu Glu Glu Glu Asp Ser	110	115	120	125
Glu Glu Asp Gly Met Val Asn His Gly Asp Leu Trp Gly Ser Glu	125	130	135	140
Asp Asp Ala Asp Thr Val Asp Asp Tyr Gly Ala Asp Ser Asn Ser	140	145	150	155
Glu Asp Glu Glu Gly Glu Ala Leu Leu Pro Ile Glu Arg Ala	155	160	165	170
Ala Arg Lys Gln Lys Ala Arg Glu Ala Ala Gly Ile Gln Trp	170	175	180	185
Ser Glu Glu Glu Thr Glu Asp Glu Glu Glu Lys Glu Val Thr	185	190	195	200
Pro Glu Ser Gly Pro Pro Lys Val Glu Glu Ala Asp Gly Gly Leu	200	205	210	215
Gln Ile Asn Val Asp Glu Glu Pro Phe Val Leu Pro Pro Ala Gly	215	220	225	230
Glu Met Glu Gln Asp Ala Gln Ala Pro Asp Leu Gln Arg Val His	230	235	240	245
Lys Arg Ile Gln Asp Ile Val Gly Ile Leu Arg Asp Phe Gly Ala	245	250	255	260
Gln Arg Glu Glu Gly Arg Ser Arg Ser Glu Tyr Leu Asn Arg Leu	260	265	270	275
Lys Lys Asp Leu Ala Ile Tyr Tyr Ser Tyr Gly Asp Phe Leu Leu	275	280	285	290
Gly Lys Leu Met Asp Leu Phe Pro Leu Ser Glu Leu Val Glu Phe	290	295	300	305
Leu Glu Ala Asn Glu Val Pro Arg Pro Val Thr Leu Arg Thr Asn	305	310	315	

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Thr Leu Lys Thr Arg Arg Arg Asp Leu Ala Gln Ala Leu Ile Asn
 320 330
 Arg Gly Val Asn Leu Asp Pro Leu Gly Lys Trp Ser Lys Thr Gly
 335 340
 Leu Val Val Tyr Asp Ser Ser Val Pro Ile Gly Ala Thr Pro Glu
 350 355
 Tyr Leu Ala Gly His Tyr Met Leu Gln Gly Ala Ser Ser Met Leu
 365 370
 Pro Val Met Ala Leu Ala Pro Gln Glu His Glu Arg Ile Leu Asp
 380 385
 Met Cys Cys Ala Pro Gly Gly Lys Thr Ser Tyr Met Ala Gln Leu
 395 400
 Met Lys Asn Thr Gly Val Ile Leu Ala Asn Asp Ala Asn Ala Glu
 410 415
 Arg Leu Lys Ser Val Val Gly Asn Leu His Arg Leu Gly Val Thr
 425 430
 Asn Thr Ile Ile Ser His Tyr Asp Gly Arg Gln Phe Pro Lys Val
 440 445
 Val Gly Gly Phe Asp Arg Val Leu Leu Asp Ala Pro Cys Ser Gly
 455 460
 Thr Gly Val Ile Ser Lys Asp Pro Ala Val Lys Thr Asn Lys Asp
 470 475
 Glu Lys Asp Ile Leu Arg Cys Ala His Leu Gln Lys Glu Leu Leu
 485 490
 Leu Ser Ala Ile Asp Ser Val Asn Ala Thr Ser Lys Thr Gly Gly
 500 505
 Tyr Leu Val Tyr Cys Thr Cys Ser Ile Thr Val Glu Glu Asn Glu
 515 520
 Trp Val Val Asp Tyr Ala Leu Lys Lys Arg Asn Val Arg Leu Val
 530 535
 Pro Thr Gly Leu Asp Phe Gly Gln Glu Gly Phe Thr Arg Phe Arg
 545 550
 Glu Arg Arg Phe His Pro Ser Leu Arg Ser Thr Arg Arg Phe Tyr
 560 565
 Pro His Thr His Asn Met Asp Gly Phe Phe Ile Ala Lys Phe Lys
 575 580
 Lys Phe Ser Asn Ser Ile Pro Gln Ser Gln Thr Gly Asn Ser Glu
 590 595
 Thr Ala Thr Pro Thr Asn Val Asp Leu Pro Gln Val Ile Pro Lys
 605 610
 Ser Glu Asn Ser Ser Gln Pro Ala Lys Lys Ala Lys Gly Ala Ala
 620 625
 Lys Thr Lys Gln Gln Leu Gln Lys Gln Gln His Pro Lys Lys Ala
 635 640
 Ser Phe Gln Lys Leu Asn Gly Ile Ser Lys Gly Ala Asp Ser Glu
 650 655
 Leu Ser Thr Val Pro Ser Val Thr Lys Thr Gln Ala Ser Ser Ser
 665 670
 Phe Gln Asp Ser Ser Gln Pro Ala Gly Lys Ala Glu Gly Ile Arg
 680 685
 Glu Pro Lys Val Thr Gly Lys Leu Lys Gln Arg Ser Pro Lys Leu
 695 700
 Gln Ser Ser Lys Lys Val Ala Phe Leu Arg Gln Asn Ala Pro Pro
 710 715
 Lys Gly Thr Asp Thr Gln Thr Pro Ala Val Leu Ser Pro Ser Lys
 725 730
 Thr Gln Ala Thr Leu Lys Pro Lys Asp His His Gln Pro Leu Gly
 740 745
 Arg Ala Lys Gly Val Glu Lys Gln Gln Leu Pro Glu Gln Pro Phe
 755 760
 Glu Lys Ala Ala Phe Gln Lys Gln Asn Asp Thr Pro Lys Gly Pro
 770 775
 Gln Pro Pro Thr Val Ser Pro Ile Arg Ser Ser Arg Pro Pro Pro

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Ala Lys Arg Lys	785	Ser Gln Ser Arg	790	Gly Asn Ser Gln Leu	795
	800		805		810
Leu Ser					

<210> 44
 <211> 537
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2959521CD1

<400> 44
 Met Arg Gly Val Gly Ala Arg Val Tyr Ala Asp Ala Pro Ala Lys
 1 5 10 15
 Leu Leu Leu Pro Pro Ala Ala Trp Asp Leu Ala Val Arg Leu
 20 25 30
 Arg Gly Ala Glu Ala Ser Glu Arg Gln Val Tyr Ser Val Thr
 35 40 45
 Met Lys Leu Leu Leu His Pro Ala Phe Gln Ser Cys Leu Leu
 50 55 60
 Leu Thr Leu Leu Gly Leu Trp Arg Thr Thr Pro Glu Ala His Ala
 65 70 75
 Ser Ser Leu Gly Ala Pro Ala Ile Ser Ala Ala Ser Phe Leu Gln
 80 85 90
 Asp Leu Ile His Arg Tyr Gly Glu Gly Asp Ser Leu Thr Leu Gln
 95 100 105
 Gln Leu Lys Ala Leu Leu Asn His Leu Asp Val Gly Val Gly Arg
 110 115 120
 Gly Asn Val Thr Gln His Val Gln Gly His Arg Asn Leu Ser Thr
 125 130 135
 Cys Phe Ser Ser Gly Asp Leu Phe Thr Ala His Asn Phe Ser Glu
 140 145 150
 Gln Ser Arg Ile Gly Ser Ser Glu Leu Gln Glu Phe Cys Pro Thr
 155 160 165
 Ile Leu Gln Gln Leu Asp Ser Arg Ala Cys Thr Ser Glu Asn Gln
 170 175 180
 Glu Asn Glu Glu Asn Glu Gln Thr Glu Glu Gly Arg Pro Ser Ala
 185 190 195
 Val Glu Val Trp Gly Tyr Gly Leu Leu Cys Val Thr Val Ile Ser
 200 205 210
 Leu Cys Ser Leu Leu Gly Ala Ser Val Val Pro Phe Met Lys Lys
 215 220 225
 Thr Phe Tyr Lys Arg Leu Leu Leu Tyr Phe Ile Ala Leu Ala Ile
 230 235 240
 Gly Thr Leu Tyr Ser Asn Ala Leu Phe Gln Leu Ile Pro Glu Ala
 245 250 255
 Phe Gly Phe Asn Pro Leu Glu Asp Tyr Tyr Val Ser Lys Ser Ala
 260 265 270
 Val Val Phe Gly Gly Phe Tyr Leu Phe Phe Thr Glu Lys Ile
 275 280 285
 Leu Lys Ile Leu Leu Lys Gln Lys Asn Glu His His His Gly His
 290 295 300
 Ser His Tyr Ala Ser Glu Ser Leu Pro Ser Lys Lys Asp Gln Glu
 305 310 315
 Glu Gly Val Met Glu Lys Leu Gln Asn Gly Asp Leu Asp His Met
 320 325 330
 Ile Pro Gln His Cys Ser Ser Glu Leu Asp Gly Lys Ala Pro Met
 335 340 345
 Val Asp Glu Lys Val Ile Val Gly Ser Leu Ser Val Gln Asp Leu
 350 355 360

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Gln	Ala	Ser	Gln	Ser	Ala	Cys	Tyr	Trp	Leu	Lys	Gly	Val	Arg	Tyr	
				365											375
Ser	Asp	Ile	Gly	Thr	Leu	Ala	Trp	Met	Ile	Thr	Leu	Ser	Asp	Gly	
				380											390
Leu	His	Asn	Phe	Ile	Asp	Gly	Leu	Ala	Ile	Gly	Ala	Ser	Phe	Thr	
				395											405
Val	Ser	Val	Phe	Gln	Gly	Ile	Ser	Thr	Ser	Val	Ala	Ile	Leu	Cys	
				410											420
Glu	Glu	Phe	Pro	His	Glu	Leu	Gly	Asp	Phe	Val	Ile	Leu	Leu	Asn	
				425											435
Ala	Gly	Met	Ser	Ile	Gln	Gln	Ala	Leu	Phe	Phe	Asn	Phe	Leu	Ser	
				440											450
Ala	Cys	Cys	Cys	Tyr	Leu	Gly	Leu	Ala	Phe	Gly	Ile	Leu	Ala	Gly	
				455											465
Ser	His	Phe	Ser	Ala	Asn	Trp	Ile	Phe	Ala	Leu	Ala	Gly	Gly	Met	
				470											480
Phe	Leu	Tyr	Ile	Ser	Leu	Ala	Asp	Met	Phe	Pro	Glu	Met	Asn	Glu	
				485											495
Val	Cys	Gln	Glu	Asp	Glu	Arg	Lys	Gly	Ser	Ile	Leu	Ile	Pro	Phe	
				500											510
Ile	Ile	Gln	Asn	Leu	Gly	Leu	Leu	Thr	Gly	Phe	Thr	Ile	Met	Val	
				515											525
Val	Leu	Thr	Met	Tyr	Ser	Gly	Gln	Ile	Gln	Ile	Gly				
				530											535

<210> 45

<211> 584

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 3082014CD1

<400> 45

Met	Leu	Trp	Gly	Gly	Arg	Val	Gly	Leu	Thr	Gly	Val	Phe	Gln	Ser	
				5											15
Leu	Ser	Tyr	Arg	Gly	Lys	Cys	Ser	Val	Thr	Leu	Leu	Asn	Glu	Thr	
				20											30
Asp	Ile	Leu	Ser	Gln	Tyr	Leu	Glu	Lys	Glu	Asp	Cys	Phe	Phe	Tyr	
				35											45
Ser	Leu	Val	Phe	Asp	Pro	Val	Gln	Lys	Thr	Leu	Leu	Ala	Asp	Gln	
				50											60
Gly	Glu	Ile	Arg	Val	Gly	Cys	Lys	Tyr	Gln	Ala	Glu	Ile	Pro	Asp	
				65											75
Arg	Leu	Val	Glu	Gly	Glu	Ser	Asp	Asn	Arg	Asn	Gln	Gln	Lys	Met	
				80											90
Glu	Met	Lys	Val	Trp	Asp	Pro	Asp	Asn	Pro	Leu	Thr	Asp	Arg	Gln	
				95											105
Ile	Asp	Gln	Phe	Leu	Val	Val	Ala	Arg	Ala	Val	Gly	Thr	Phe	Ala	
				110											120
Arg	Ala	Leu	Asp	Cys	Ser	Ser	Ser	Ile	Arg	Gln	Pro	Ser	Leu	His	
				125											135
Met	Ser	Ala	Ala	Ala	Ala	Ser	Arg	Asp	Ile	Thr	Leu	Phe	His	Ala	
				140											150
Met	Asp	Thr	Leu	Gln	Arg	Asn	Gly	Tyr	Asp	Leu	Ala	Lys	Ala	Met	
				155											165
Ser	Thr	Leu	Val	Pro	Gln	Gly	Gly	Pro	Val	Leu	Cys	Arg	Asp	Glu	
				170											180
Met	Glu	Glu	Trp	Ser	Ala	Ser	Glu	Ala	Met	Leu	Phe	Glu	Glu	Ala	
				185											195
Leu	Glu	Lys	Tyr	Gly	Lys	Asp	Phe	Asn	Asp	Ile	Arg	Gln	Asp	Phe	
				200											210
Leu	Pro	Trp	Lys	Ser	Leu	Ala	Ser	Ile	Val	Gln	Phe	Tyr	Tyr	Met	

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Trp Lys Thr Thr	215	Asp Arg Tyr Ile Gln	220	Gln Lys Arg Leu Lys	225
Ala Glu Ala Asp	230	Ser Lys Leu Lys Gln	235	Val Tyr Ile Pro Thr	240
Thr Lys Pro Asn	245	Pro Asn Gln Ile Ile	250	Ser Val Gly Ser Lys	255
Gly Met Asn Gly	260	Ala Gly Phe Gln Lys	265	Gly Leu Thr Cys Glu	270
Cys His Thr Thr	275	Gln Ser Ala Gln Trp	280	Tyr Ala Trp Gly Pro	285
Asn Met Gln Cys	290	Arg Leu Cys Ala Ser	295	Cys Trp Ile Tyr Trp	300
Lys Tyr Gly Gly	305	Leu Lys Thr Pro Thr	310	Gln Leu Glu Gly Ala	315
Arg Gly Thr Thr	320	Glu Pro His Ser Arg	325	Gly His Leu Ser Arg	330
Glu Ala Gln Ser	335	Leu Ser Pro Tyr Thr	340	Thr Ser Ala Asn Arg	345
Lys Leu Leu Ala	350	Lys Asn Arg Gln Thr	355	Phe Leu Leu Gln Thr	360
Lys Leu Thr Arg	365	Leu Ala Arg Arg Met	370	Cys Arg Asp Leu Leu	375
Pro Arg Arg Ala	380	Ala Arg Arg Pro Tyr	385	Ala Pro Ile Asn Ala	390
Ala Ile Lys Ala	395	Glu Cys Ser Ile Arg	400	Leu Pro Lys Ala Ala	405
Thr Pro Leu Lys	410	Ile His Pro Leu Val	415	Arg Leu Pro Leu Ala	420
Ile Val Lys Asp	425	Leu Val Ala Gln Ala	430	Pro Leu Lys Pro Lys	435
Pro Arg Gly Thr	440	Lys Thr Pro Ile Asn	445	Arg Asn Gln Leu Ser	450
Asn Arg Gly Leu	455	Gly Gly Ile Met Val	460	Lys Arg Ala Tyr Glu	465
Met Ala Gly Ala	470	Gly Val Pro Phe Ser	475	Ala Asn Gly Arg Pro	480
Ala Ser Gly Ile	485	Arg Ser Ser Ser Gln	490	Pro Ala Ala Lys Arg	495
Lys Leu Asn Pro	500	Ala Asp Ala Pro Asn	505	Pro Val Val Phe Val	510
Thr Lys Asp Thr	515	Arg Ala Leu Arg Lys	520	Ala Leu Thr His Leu	525
Met Arg Arg Ala	530	Ala Arg Arg Pro Asn	535	Leu Pro Leu Lys Val	540
Pro Thr Leu Ile	545	Ala Val Arg Pro Pro	550	Val Pro Leu Pro Ala	555
Ser His Pro Ala	560	Ser Thr Asn Glu Pro	565	Ile Val Leu Glu Asp	570
	575		580		

<210> 46
 <211> 425
 <212> PRT
 <213> Homo sapiens

 <220>
 <221> misc_feature
 <223> Incyte ID No: 3520701CD1

 <400> 46
 Met Ala Gly Ala Glu Gly Ala Ala Gly Arg Gln Ser Glu Leu Glu
 1 5 10 15
 Pro Val Val Ser Leu Val Asp Val Leu Glu Glu Asp Glu Glu Leu
 20 25 30

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Glu Asn Glu Ala Cys Ala Val Leu Gly Gly Ser Asp Ser Glu Lys
 35 40
 Cys Ser Tyr Ser Gln Gly Ser Val Lys Arg Gln Ala Leu Tyr Ala
 50 55 60
 Cys Ser Thr Cys Thr Pro Glu Gly Glu Glu Pro Ala Gly Ile Cys
 65 70 75
 Leu Ala Cys Ser Tyr Glu Cys His Gly Ser His Lys Leu Phe Glu
 80 85 90
 Leu Tyr Thr Lys Arg Asn Phe Arg Cys Asp Cys Gly Asn Ser Lys
 95 100 105
 Phe Lys Asn Leu Glu Cys Lys Leu Leu Pro Asp Lys Ala Lys Val
 110 115 120
 Asn Ser Gly Asn Lys Tyr Asn Asp Asn Phe Phe Gly Leu Tyr Cys
 125 130 135
 Ile Cys Lys Arg Pro Tyr Pro Asp Pro Glu Asp Glu Ile Pro Asp
 140 145 150
 Glu Met Ile Gln Cys Val Val Cys Glu Asp Trp Phe His Gly Arg
 155 160 165
 His Leu Gly Ala Ile Pro Pro Glu Ser Gly Asp Phe Gln Glu Met
 170 175 180
 Val Cys Gln Ala Cys Met Lys Arg Cys Ser Phe Leu Trp Ala Tyr
 185 190 195
 Ala Ala Gln Leu Ala Val Thr Lys Ile Ser Thr Glu Asp Asp Gly
 200 205 210
 Leu Val Arg Asn Ile Asp Gly Ile Gly Asp Gln Glu Val Ile Lys
 215 220 225
 Pro Glu Asn Gly Glu His Gln Asp Ser Thr Leu Lys Glu Asp Val
 230 235 240
 Pro Glu Gln Gly Lys Asp Asp Val Arg Glu Val Lys Val Glu Gln
 245 250 255
 Asn Ser Glu Pro Cys Ala Gly Ser Ser Ser Glu Ser Asp Leu Gln
 260 265 270
 Thr Val Phe Lys Asn Glu Ser Leu Asn Ala Glu Ser Lys Ser Gly
 275 280 285
 Cys Lys Leu Gln Glu Leu Lys Ala Lys Gln Leu Ile Lys Lys Asp
 290 295 300
 Thr Ala Thr Tyr Trp Pro Leu Asn Trp Arg Ser Lys Leu Cys Thr
 305 310 315
 Cys Gln Asp Cys Met Lys Met Tyr Gly Asp Leu Asp Val Leu Phe
 320 325 330
 Leu Thr Asp Glu Tyr Asp Thr Val Leu Ala Tyr Glu Asn Lys Gly
 335 340 345
 Lys Ile Ala Gln Ala Thr Asp Arg Ser Asp Pro Leu Met Asp Thr
 350 355 360
 Leu Ser Ser Met Asn Arg Val Gln Gln Val Glu Leu Ile Cys Glu
 365 370 375
 Tyr Asn Asp Leu Lys Thr Glu Leu Lys Asp Tyr Leu Lys Arg Phe
 380 385 390
 Ala Asp Glu Gly Thr Val Val Lys Arg Glu Asp Ile Gln Gln Phe
 395 400 405
 Phe Glu Glu Phe Gln Ser Lys Lys Arg Arg Arg Val Asp Gly Met
 410 415 420
 Gln Tyr Tyr Cys Ser 425

<210> 47

<211> 255

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 4184320CD1

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<400> 47

Met	Tyr	Val	Arg	Val	Ser	Phe	Asp	Thr	Lys	Pro	Asp	Leu	Leu	Leu
1				5					10					15
His	Leu	Met	Thr	Lys	Glu	Trp	Gln	Leu	Glu	Leu	Pro	Lys	Leu	Leu
				20					25					30
Ile	Ser	Val	His	Gly	Gly	Leu	Gln	Asn	Phe	Glu	Leu	Gln	Pro	Lys
				35					40					45
Leu	Lys	Gln	Val	Phe	Gly	Lys	Gly	Leu	Ile	Lys	Ala	Ala	Met	Thr
				50					55					60
Thr	Gly	Ala	Trp	Ile	Phe	Thr	Gly	Gly	Val	Asn	Thr	Gly	Val	Ile
				65					70					75
Arg	His	Val	Gly	Asp	Ala	Leu	Lys	Asp	His	Ala	Ser	Lys	Ser	Arg
				80					85					90
Gly	Lys	Ile	Cys	Thr	Ile	Gly	Ile	Ala	Pro	Trp	Gly	Ile	Val	Glu
				95					100					105
Asn	Gln	Glu	Asp	Leu	Ile	Gly	Arg	Asp	Val	Val	Arg	Pro	Tyr	Gln
				110					115					120
Thr	Met	Ser	Asn	Pro	Met	Ser	Lys	Leu	Thr	Val	Leu	Asn	Ser	Met
				125					130					135
His	Ser	His	Phe	Ile	Leu	Ala	Asp	Asn	Gly	Thr	Thr	Gly	Lys	Tyr
				140					145					150
Gly	Ala	Glu	Val	Lys	Leu	Arg	Arg	Gln	Leu	Glu	Lys	His	Ile	Ser
				155					160					165
Leu	Gln	Lys	Ile	Asn	Thr	Arg	Cys	Leu	Pro	Phe	Phe	Ser	Leu	Asp
				170					175					180
Ser	Arg	Leu	Phe	Tyr	Ser	Phe	Trp	Gly	Ser	Cys	Gln	Leu	Asp	Ser
				185					190					195
Val	Gly	Ile	Gly	Gln	Gly	Val	Pro	Val	Val	Ala	Leu	Ile	Val	Glu
				200					205					210
Gly	Gly	Pro	Asn	Val	Ile	Ser	Ile	Val	Leu	Glu	Tyr	Leu	Arg	Asp
				215					220					225
Thr	Pro	Pro	Val	Pro	Val	Val	Val	Cys	Asp	Gly	Ser	Gly	Arg	Ala
				230					235					240
Ser	Asp	Ile	Leu	Ala	Phe	Gly	His	Lys	Tyr	Ser	Glu	Glu	Gly	Gly
				245					250					255

<210> 48

<211> 111

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 4764233CD1

<400> 48

Met	Ser	Trp	Arg	Gly	Arg	Ser	Thr	Tyr	Arg	Pro	Arg	Pro	Arg	Arg
1				5					10					15
Ser	Leu	Gln	Pro	Pro	Glu	Leu	Ile	Gly	Ala	Met	Leu	Glu	Pro	Thr
				20					25					30
Asp	Glu	Glu	Pro	Lys	Glu	Glu	Lys	Pro	Pro	Thr	Lys	Ser	Arg	Asn
				35					40					45
Pro	Thr	Pro	Asp	Gln	Lys	Arg	Glu	Asp	Asp	Gln	Gly	Ala	Ala	Glu
				50					55					60
Ile	Gln	Val	Pro	Asp	Leu	Glu	Ala	Asp	Leu	Gln	Glu	Leu	Cys	Gln
				65					70					75
Thr	Lys	Thr	Gly	Asp	Gly	Cys	Glu	Gly	Gly	Thr	Asp	Val	Lys	Gly
				80					85					90
Lys	Ile	Leu	Pro	Lys	Ala	Glu	His	Phe	Lys	Met	Pro	Glu	Ala	Gly
				95					100					105
Glu	Gly	Lys	Ser	Gln	Val									
				110										

<210> 49

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<211> 422

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 4817352CD1

<400> 49

Met Gly Lys Ala Lys Val Pro Ala Ser Lys Arg Ala Pro Ser Ser	
1 5 10 15	
Pro Val Ala Lys Pro Gly Pro Val Lys Thr Leu Thr Arg Lys Lys	
20 25 30	
Asn Lys Lys Lys Lys Arg Phe Trp Lys Ser Lys Ala Arg Glu Val	
35 40 45	
Ser Lys Lys Pro Ala Ser Gly Pro Gly Ala Val Val Arg Pro Pro	
50 55 60	
Lys Ala Pro Glu Asp Phe Ser Gln Asn Trp Lys Ala Leu Gln Glu	
65 70 75	
Trp Leu Leu Lys Gln Lys Ser Gln Ala Pro Glu Lys Pro Leu Val	
80 85 90	
Ile Ser Gln Met Gly Ser Lys Lys Lys Pro Lys Ile Ile Gln Gln	
95 100 105	
Asn Lys Lys Glu Thr Ser Pro Gln Val Lys Gly Glu Glu Met Pro	
110 115 120	
Ala Gly Lys Asp Gln Glu Ala Ser Arg Gly Ser Val Pro Ser Gly	
125 130 135	
Ser Lys Met Asp Arg Arg Ala Pro Val Pro Arg Thr Lys Ala Ser	
140 145 150	
Gly Thr Glu His Asn Lys Lys Gly Thr Lys Glu Arg Thr Asn Gly	
155 160 165	
Asp Ile Val Pro Glu Arg Gly Asp Ile His Lys Lys Arg Lys	
170 175 180	
Ala Lys Glu Ala Ala Pro Ala Pro Pro Thr Glu Glu Asp Ile Trp	
185 190 195	
Phe Asp Asp Val Asp Pro Ala Asp Ile Glu Ala Ala Ile Gly Pro	
200 205 210	
Glu Ala Ala Lys Ile Ala Arg Lys Gln Leu Gly Gln Ser Glu Gly	
215 220 225	
Ser Val Ser Leu Ser Leu Val Lys Glu Gln Ala Phe Gly Gly Leu	
230 235 240	
Thr Arg Ala Leu Ala Leu Asp Cys Glu Met Val Gly Val Gly Pro	
245 250 255	
Lys Gly Glu Glu Ser Met Ala Ala Arg Val Ser Ile Val Asn Gln	
260 265 270	
Tyr Gly Lys Cys Val Tyr Asp Lys Tyr Val Lys Pro Thr Glu Pro	
275 280 285	
Val Thr Asp Tyr Arg Thr Ala Val Ser Gly Ile Arg Pro Glu Asn	
290 295 300	
Leu Lys Gln Gly Glu Glu Leu Glu Val Val Gln Lys Glu Val Ala	
305 310 315	
Glu Met Leu Lys Gly Arg Ile Leu Val Gly His Ala Leu His Asn	
320 325 330	
Asp Leu Lys Val Leu Phe Leu Asp His Pro Lys Lys Lys Ile Arg	
335 340 345	
Asp Thr Gln Lys Tyr Lys Pro Phe Lys Ser Gln Val Lys Ser Gly	
350 355 360	
Arg Pro Ser Leu Arg Leu Leu Ser Glu Lys Ile Leu Gly Leu Gln	
365 370 375	
Val Gln Gln Ala Glu His Cys Ser Ile Gln Asp Ala Gln Ala Ala	
380 385 390	
Met Arg Leu Tyr Val Met Val Lys Lys Glu Trp Glu Ser Met Ala	
395 400 405	

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Arg Asp Arg Arg Pro Leu Leu Thr Ala Pro Asp His Cys Ser Asp
410 415 420

Asp Ala

<210> 50

<211> 397

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5040573CD1

<400> 50

Met	Ala	Met	Ile	Glu	Leu	Gly	Phe	Gly	Arg	Gln	Asn	Phe	His	Pro
1				5					10					15
Leu	Lys	Arg	Lys	Ser	Ser	Leu	Leu	Leu	Lys	Leu	Ile	Ala	Val	Val
				20					25					30
Phe	Ala	Val	Leu	Leu	Phe	Cys	Glu	Phe	Leu	Ile	Tyr	Tyr	Leu	Ala
				35					40					45
Ile	Phe	Gln	Cys	Asn	Trp	Pro	Glu	Val	Lys	Thr	Thr	Ala	Ser	Asp
				50					55					60
Gly	Glu	Gln	Thr	Thr	Arg	Glu	Pro	Val	Leu	Lys	Ala	Met	Phe	Leu
				65					70					75
Ala	Asp	Thr	His	Leu	Leu	Gly	Glu	Phe	Leu	Gly	His	Trp	Leu	Asp
				80					85					90
Lys	Leu	Arg	Arg	Glu	Trp	Gln	Met	Glu	Arg	Ala	Phe	Gln	Thr	Ala
				95					100					105
Leu	Trp	Leu	Leu	Gln	Pro	Glu	Val	Val	Phe	Ile	Leu	Gly	Asp	Ile
				110					115					120
Phe	Asp	Glu	Gly	Lys	Trp	Ser	Thr	Pro	Glu	Ala	Trp	Ala	Asp	Asp
				125					130					135
Val	Glu	Arg	Phe	Gln	Lys	Met	Phe	Arg	His	Pro	Ser	His	Val	Gln
				140					145					150
Leu	Lys	Val	Val	Ala	Gly	Asn	His	Asp	Ile	Gly	Phe	His	Tyr	Glu
				155					160					165
Met	Asn	Thr	Tyr	Lys	Val	Glu	Arg	Phe	Glu	Lys	Val	Phe	Ser	Ser
				170					175					180
Glu	Arg	Leu	Phe	Ser	Trp	Lys	Gly	Ile	Asn	Phe	Val	Met	Val	Asn
				185					190					195
Ser	Val	Ala	Leu	Asn	Gly	Asp	Gly	Cys	Gly	Ile	Cys	Ser	Glu	Thr
				200					205					210
Glu	Ala	Glu	Leu	Ile	Glu	Val	Ser	His	Arg	Leu	Asn	Cys	Ser	Arg
				215					220					225
Glu	Gln	Ala	Arg	Gly	Ser	Ser	Arg	Cys	Gly	Pro	Gly	Pro	Leu	Leu
				230					235					240
Pro	Thr	Ser	Ala	Pro	Val	Leu	Leu	Gln	His	Tyr	Pro	Leu	Tyr	Arg
				245					250					255
Arg	Ser	Asp	Ala	Asn	Cys	Ser	Gly	Glu	Asp	Ala	Ala	Pro	Pro	Glu
				260					265					270
Glu	Arg	Asp	Ile	Pro	Phe	Lys	Glu	Asn	Tyr	Asp	Val	Leu	Ser	Arg
				275					280					285
Glu	Ala	Ser	Gln	Lys	Leu	Leu	Trp	Trp	Leu	Gln	Pro	Arg	Leu	Val
				290					295					300
Leu	Ser	Gly	His	Thr	His	Ser	Ala	Cys	Glu	Val	His	His	Gly	Gly
				305					310					315
Arg	Val	Pro	Glu	Leu	Ser	Val	Pro	Ser	Phe	Ser	Trp	Arg	Asn	Arg
				320					325					330
Asn	Asn	Pro	Ser	Phe	Ile	Met	Gly	Ser	Ile	Thr	Pro	Thr	Asp	Tyr
				335					340					345
Thr	Leu	Ser	Lys	Cys	Tyr	Leu	Pro	Arg	Glu	Asp	Val	Val	Leu	Ile
				350					355					360
Ile	Tyr	Cys	Gly	Val	Val	Gly	Phe	Leu	Val	Val	Leu	Thr	Leu	Thr

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His Phe Gly Leu	365	Leu Ala Ser Pro Phe	370	Leu Ser Gly Leu Asn	375
	380		385		390
Leu Gly Lys Arg		Lys Thr Arg			
	395				

<210> 51

<211> 800

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5627029CD1

<400> 51

Met Gly Ser Ser Lys Lys His Arg Gly Glu Lys Glu Ala Ala Gly	1	5	10	15
Thr Thr Ala Ala Ala Gly Thr Gly Gly Ala Thr Glu Gln Pro Pro	20	25	30	35
Arg His Arg Glu His Lys Lys His Lys His Arg Ser Gly Gly Ser	35	40	45	50
Gly Gly Ser Gly Gly Glu Arg Arg Lys Arg Ser Arg Glu Arg Gly	50	55	60	65
Gly Glu Arg Gly Ser Gly Arg Arg Gly Ala Glu Ala Glu Ala Arg	65	70	75	80
Ser Ser Thr His Gly Arg Glu Arg Ser Gln Ala Glu Pro Ser Glu	80	85	90	95
Arg Arg Val Lys Arg Glu Lys Arg Asp Asp Gly Tyr Glu Ala Ala	95	100	105	110
Ala Ser Ser Lys Thr Ser Ser Gly Asp Ala Ser Ser Leu Ser Ile	110	115	120	125
Glu Glu Thr Asn Lys Leu Arg Ala Lys Leu Gly Leu Lys Pro Leu	125	130	135	140
Glu Val Asn Ala Ile Lys Lys Glu Ala Gly Thr Lys Glu Glu Pro	140	145	150	155
Val Thr Ala Asp Val Ile Asn Pro Met Ala Leu Arg Gln Arg Glu	155	160	165	170
Glu Leu Arg Glu Lys Leu Ala Ala Ala Lys Glu Lys Arg Leu Leu	170	175	180	185
Asn Gln Lys Leu Gly Lys Ile Lys Thr Leu Gly Glu Asp Asp Pro	185	190	195	200
Trp Leu Asp Asp Thr Ala Ala Trp Ile Glu Arg Ser Arg Gln Leu	200	205	210	215
Gln Lys Glu Lys Asp Leu Ala Glu Lys Arg Ala Lys Leu Leu Glu	215	220	225	230
Glu Met Asp Gln Glu Phe Gly Val Ser Thr Leu Val Glu Glu Glu	230	235	240	245
Phe Gly Gln Arg Arg Gln Asp Leu Tyr Ser Ala Arg Asp Leu Gln	245	250	255	260
Gly Leu Thr Val Glu His Ala Ile Asp Ser Phe Arg Glu Gly Glu	260	265	270	275
Thr Met Ile Leu Thr Leu Lys Asp Lys Gly Val Leu Gln Glu Glu	275	280	285	290
Glu Asp Val Leu Val Asn Val Asn Leu Val Asp Lys Glu Arg Ala	290	295	300	305
Glu Lys Asn Val Glu Leu Arg Lys Lys Lys Pro Asp Tyr Leu Pro	305	310	315	320
Tyr Ala Glu Asp Glu Ser Val Asp Asp Leu Ala Gln Gln Lys Pro	320	325	330	335
Arg Ser Ile Leu Ser Lys Tyr Asp Glu Glu Glu Gly Glu Arg	335	340	345	350
Pro His Ser Phe Arg Leu Glu Gln Gly Gly Thr Ala Asp Gly Leu	350	355	360	

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Arg Glu Arg Glu Leu Glu Glu Ile Arg Ala Lys Leu Arg Leu Gln
 365 375
 Ala Gln Ser Leu Ser Thr Val Gly Pro Arg Leu Ala Ser Glu Tyr
 380 385
 Leu Thr Pro Glu Glu Met Val Thr Phe Lys Lys Thr Lys Arg Arg
 395 400
 Val Lys Lys Ile Arg Lys Lys Glu Lys Glu Val Val Val Arg Ala
 410 415
 Asp Asp Leu Leu Pro Leu Gly Asp Gln Thr Gln Asp Gly Asp Phe
 425 430
 Gly Ser Arg Leu Arg Gly Arg Gly Arg Arg Arg Val Ser Glu Val
 440 445
 Glu Glu Glu Lys Glu Pro Val Pro Gln Pro Leu Pro Ser Asp Asp
 455 460
 Thr Arg Val Glu Asn Met Asp Ile Ser Asp Glu Glu Glu Gly Gly
 470 475
 Ala Pro Pro Pro Ala Ser Pro Gln Val Leu Glu Glu Asp Glu Ala
 485 490
 Glu Leu Glu Leu Gln Lys Gln Leu Glu Lys Gly Arg Arg Leu Arg
 500 505
 Gln Leu Gln Gln Leu Gln Gln Leu Arg Asp Ser Gly Glu Lys Val
 515 520
 Val Glu Ile Val Lys Lys Leu Glu Ser Arg Gln Arg Gly Trp Glu
 530 535
 Glu Asp Glu Asp Pro Glu Arg Lys Gly Ala Ile Val Phe Asn Ala
 545 550
 Thr Ser Glu Phe Cys Arg Thr Leu Gly Glu Ile Pro Thr Tyr Gly
 560 565
 Leu Ala Gly Asn Arg Glu Glu Gln Glu Glu Leu Met Asp Phe Glu
 575 580
 Arg Asp Glu Glu Arg Ser Ala Asn Gly Gly Ser Glu Ser Asp Gly
 590 595
 Glu Glu Asn Ile Gly Trp Ser Thr Val Asn Leu Asp Glu Glu Lys
 605 610
 Gln Gln Gln Asp Phe Ser Ala Ser Ser Thr Thr Ile Leu Asp Glu
 620 625
 Glu Pro Ile Val Asn Arg Gly Leu Ala Ala Ala Leu Leu Leu Cys
 635 640
 Gln Asn Lys Gly Leu Leu Glu Thr Thr Val Gln Lys Val Ala Arg
 650 655
 Val Lys Ala Pro Asn Lys Ser Leu Pro Ser Ala Val Tyr Cys Ile
 665 670
 Glu Asp Lys Met Ala Ile Asp Asp Lys Tyr Ser Arg Arg Glu Glu
 680 685
 Tyr Arg Gly Phe Thr Gln Asp Phe Lys Glu Lys Asp Gly Tyr Lys
 695 700
 Pro Asp Val Lys Ile Glu Tyr Val Asp Glu Thr Gly Arg Lys Leu
 710 715
 Thr Pro Lys Glu Ala Phe Arg Gln Leu Ser His Arg Phe His Gly
 725 730
 Lys Gly Ser Gly Lys Met Lys Thr Glu Arg Arg Met Lys Lys Leu
 740 745
 Asp Glu Glu Ala Leu Leu Lys Lys Met Ser Ser Ser Asp Thr Pro
 755 760
 Leu Gly Thr Val Ala Leu Leu Gln Glu Lys Gln Lys Ala Gln Lys
 770 775
 Thr Pro Tyr Ile Val Leu Ser Gly Ser Gly Lys Ser Met Asn Ala
 785 790
 Asn Thr Ile Thr Lys 800

<210> 52
 <211> 713
 <212> PRT

WO 01/07471

PCT/US00/19948

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5678487CD1

<400> 52

Met	Ala	Lys	Ser	Pro	Glu	Asn	Ser	Thr	Leu	Glu	Glu	Ile	Leu	Gly	
1				5					10					15	
Gln	Tyr	Gln	Arg	Ser	Leu	Arg	Glu	His	Ala	Ser	Arg	Ser	Ile	His	
				20					25					30	
Gln	Leu	Thr	Cys	Ala	Leu	Lys	Glu	Gly	Asp	Val	Thr	Ile	Gly	Glu	
				35					40					45	
Asp	Ala	Pro	Asn	Leu	Ser	Phe	Ser	Thr	Ser	Val	Gly	Asn	Glu	Asp	
				50					55					60	
Ala	Arg	Thr	Ala	Trp	Pro	Glu	Leu	Gln	Gln	Ser	His	Ala	Val	Asn	
				65					70					75	
Gln	Leu	Lys	Asp	Leu	Leu	Arg	Gln	Gln	Ala	Asp	Lys	Glu	Ser	Glu	
				80					85					90	
Val	Ser	Pro	Ser	Arg	Arg	Arg	Lys	Met	Ser	Pro	Leu	Arg	Ser	Leu	
				95					100					105	
Glu	His	Glu	Glu	Thr	Asn	Met	Pro	Thr	Met	His	Asp	Leu	Val	His	
				110					115					120	
Thr	Ile	Asn	Asp	Gln	Ser	Gln	Tyr	Ile	His	His	Leu	Glu	Ala	Glu	
				125					130					135	
Val	Lys	Phe	Cys	Lys	Glu	Glu	Leu	Ser	Gly	Met	Lys	Asn	Lys	Ile	
				140					145					150	
Gln	Val	Val	Val	Leu	Glu	Asn	Glu	Gly	Leu	Gln	Gln	Gln	Leu	Lys	
				155					160					165	
Ser	Gln	Arg	Gln	Glu	Glu	Thr	Leu	Arg	Glu	Gln	Thr	Leu	Leu	Asp	
				170					175					180	
Ala	Ser	Gly	Asn	Met	His	Asn	Ser	Trp	Ile	Thr	Thr	Gly	Glu	Asp	
				185					190					195	
Ser	Gly	Val	Gly	Glu	Thr	Ser	Lys	Arg	Pro	Phe	Ser	His	Asp	Asn	
				200					205					210	
Ala	Asp	Phe	Gly	Lys	Ala	Ala	Ser	Ala	Gly	Glu	Gln	Leu	Glu	Leu	
				215					220					225	
Glu	Lys	Leu	Lys	Leu	Thr	Tyr	Glu	Glu	Lys	Cys	Glu	Ile	Glu	Glu	
				230					235					240	
Ser	Gln	Leu	Lys	Phe	Leu	Arg	Asn	Asp	Leu	Ala	Glu	Tyr	Gln	Arg	
				245					250					255	
Thr	Cys	Glu	Asp	Leu	Lys	Glu	Gln	Leu	Lys	His	Lys	Glu	Phe	Leu	
				260					265					270	
Leu	Ala	Ala	Asn	Thr	Cys	Asn	Arg	Val	Gly	Gly	Leu	Cys	Leu	Lys	
				275					280					285	
Cys	Ala	Gln	His	Glu	Ala	Val	Leu	Ser	Gln	Thr	His	Thr	Asn	Val	
				290					295					300	
His	Met	Gln	Thr	Ile	Glu	Arg	Leu	Val	Lys	Glu	Arg	Asp	Asp	Leu	
				305					310					315	
Met	Ser	Ala	Leu	Val	Ser	Val	Arg	Ser	Ser	Leu	Ala	Asp	Thr	Gln	
				320					325					330	
Gln	Arg	Glu	Ala	Ser	Ala	Tyr	Glu	Gln	Val	Lys	Gln	Val	Leu	Gln	
				335					340					345	
Ile	Ser	Glu	Glu	Ala	Asn	Phe	Glu	Lys	Thr	Lys	Ala	Leu	Ile	Gln	
				350					355					360	
Cys	Asp	Gln	Leu	Arg	Lys	Glu	Leu	Glu	Arg	Gln	Ala	Glu	Arg	Leu	
				365					370					375	
Glu	Lys	Asp	Leu	Ala	Ser	Gln	Gln	Glu	Lys	Arg	Ala	Ile	Glu	Lys	
				380					385					390	
Asp	Met	Met	Lys	Lys	Glu	Ile	Thr	Lys	Glu	Arg	Glu	Tyr	Met	Gly	
				395					400					405	
Ser	Lys	Met	Leu	Ile	Leu	Ser	Gln	Asn	Ile	Ala	Gln	Leu	Glu	Ala	
				410					415					420	

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Gln Val Glu Lys Val Thr Lys Glu Lys Ile Ser Ala Ile Asn Gln 425 435
 Leu Glu Glu Ile Gln Ser Gln Leu Ala Ser Arg Glu Met Asp Val 440 450
 Thr Lys Val Cys Gly Glu Met Arg Tyr Gln Leu Asn Lys Thr Asn 455 465
 Met Glu Lys Asp Glu Ala Glu Lys Glu His Arg Glu Phe Arg Ala 470 480
 Lys Thr Asn Arg Asp Leu Glu Ile Lys Asp Gln Glu Ile Glu Lys 485 495
 Leu Arg Ile Glu Leu Asp Glu Ser Lys Gln His Leu Glu Gln Glu 500 510
 Gln Gln Lys Ala Ala Leu Ala Arg Glu Glu Cys Leu Arg Leu Thr 515 525
 Glu Leu Leu Gly Glu Ser Glu His Gln Leu His Leu Thr Arg Gln 530 540
 Glu Lys Asp Ser Ile Gln Gln Ser Phe Ser Lys Glu Ala Lys Ala 545 555
 Gln Ala Leu Gln Ala Gln Gln Arg Glu Gln Glu Leu Thr Gln Lys 560 570
 Ile Gln Gln Met Glu Ala Gln His Asp Lys Thr Glu Asn Glu Gln 575 585
 Tyr Leu Leu Leu Thr Ser Gln Asn Thr Phe Leu Thr Lys Leu Lys 590 600
 Glu Glu Cys Cys Thr Leu Ala Lys Lys Leu Glu Gln Ile Ser Gln 605 615
 Lys Thr Arg Ser Glu Ile Ala Gln Leu Ser Gln Glu Lys Arg Tyr 620 630
 Thr Tyr Asp Lys Leu Gly Lys Leu Gln Arg Arg Asn Glu Glu Leu 635 645
 Glu Glu Gln Cys Val Gln His Gly Arg Val His Glu Thr Met Lys 650 660
 Gln Arg Leu Arg Gln Leu Asp Lys His Ser Gln Ala Thr Ala Gln 665 675
 Gln Leu Val Gln Leu Leu Ser Lys Gln Asn Gln Leu Leu Leu Glu 680 690
 Arg Gln Ser Leu Ser Glu Glu Val Asp Arg Leu Arg Thr Gln Leu 695 705
 Pro Ser Met Pro Gln Ser Asp Cys 710

<210> 53

<211> 880

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5682976CD1

<400> 53

Met Ser Arg Gly Gly Ser Cys Pro His Leu Leu Trp Asp Val Arg 1 10 15
 Lys Arg Ser Leu Gly Leu Glu Asp Pro Ser Arg Leu Arg Ser Arg 20 25 30
 Tyr Leu Gly Arg Arg Glu Phe Ile Gln Arg Leu Lys Leu Glu Ala 35 40 45
 Thr Leu Asn Val His Asp Gly Cys Val Asn Thr Ile Cys Trp Asn 50 55 60
 Asp Thr Gly Glu Tyr Ile Leu Ser Gly Ser Asp Asp Thr Lys Leu 65 70 75
 Val Ile Ser Asn Pro Tyr Ser Arg Lys Val Leu Thr Thr Ile Arg 80 85 90
 Ser Gly His Arg Ala Asn Ile Phe Ser Ala Lys Phe Leu Pro Cys

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	95		100		105
Thr Asn Asp Lys	Gln	Ile Val Ser Cys	Ser Gly Asp Gly Val	Ile	
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Phe Tyr Thr Asn Val	Glu Gln Asp Ala	Glu Thr Asn Arg Gln	Cys		
	125				135
Gln Phe Thr Cys His	Tyr Gly Thr Thr	Tyr Glu Ile Met Thr	Val		
	140				150
Pro Asn Asp Pro Tyr	Thr Phe Leu Ser Cys	Gly Glu Asp Gly	Thr		
	155				165
Val Arg Trp Phe Asp	Thr Arg Ile Lys Thr	Ser Cys Thr Lys	Glu		
	170				180
Asp Cys Lys Asp Asp	Ile Leu Ile Asn Cys	Arg Arg Ala Ala	Thr		
	185				195
Ser Val Ala Ile Cys	Pro Pro Ile Pro Tyr	Tyr Leu Ala Val	Gly		
	200				210
Cys Ser Asp Ser Ser	Val Arg Ile Tyr	Arg Arg Met Leu	Gly		
	215				225
Thr Arg Ala Thr Gly	Asn Tyr Ala Gly	Arg Gly Thr Thr	Gly		
	230				240
Val Ala Arg Phe Ile	Pro Ser His Leu Asn	Asn Lys Ser Cys	Arg		
	245				255
Val Thr Ser Leu Cys	Tyr Ser Glu Asp Gly	Gln Glu Ile Leu	Val		
	260				270
Ser Tyr Ser Ser Asp	Tyr Ile Tyr Leu Phe	Asp Pro Lys Asp	Asp		
	275				285
Thr Ala Arg Glu Leu	Lys Thr Pro Ser Ala	Glu Glu Arg Arg	Glu		
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Glu Leu Arg Gln Pro	Pro Val Lys Arg Leu	Arg Leu Arg Gly	Asp		
	305				315
Trp Ser Asp Thr Gly	Pro Arg Ala Arg Pro	Glu Ser Glu Arg	Glu		
	320				330
Arg Asp Gly Glu Gln	Ser Pro Asn Val Ser	Leu Met Gln Arg	Met		
	335				345
Ser Asp Met Leu Ser	Arg Trp Phe Glu Glu	Ala Ser Glu Val	Ala		
	350				360
Gln Ser Asn Arg Gly	Arg Gly Arg Ser Arg	Pro Arg Gly Gly	Thr		
	365				375
Ser Gln Ser Asp Ile	Ser Thr Leu Pro Thr	Val Pro Ser Ser	Pro		
	380				390
Asp Leu Glu Val Ser	Glu Thr Ala Met Glu	Val Asp Thr Pro	Ala		
	395				405
Glu Gln Phe Leu Gln	Pro Ser Thr Ser Ser	Thr Met Ser Ala	Gln		
	410				420
Ala His Ser Thr Ser	Ser Pro Thr Glu Ser	Pro His Ser Thr	Pro		
	425				435
Leu Leu Ser Ser Pro	Asp Ser Glu Gln Arg	Gln Ser Val Glu	Ala		
	440				450
Ser Gly His His Thr	His His Gln Ser Asp	Ser Pro Ser Ser	Val		
	455				465
Val Asn Lys Gln Leu	Gly Ser Met Ser Leu	Asp Glu Gln Gln	Asp		
	470				480
Asn Asn Asn Glu Lys	Leu Ser Pro Lys Pro	Gly Thr Gly Glu	Pro		
	485				495
Val Leu Ser Leu His	Tyr Ser Thr Glu Gly	Thr Thr Thr Ser	Thr		
	500				510
Ile Lys Leu Asn Phe	Thr Asp Glu Trp Ser	Ser Ile Ala Ser	Ser		
	515				525
Ser Arg Gly Ile Gly	Ser His Cys Lys Ser	Glu Gly Gln Glu	Glu		
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Ser Phe Val Pro Gln	Ser Ser Val Gln Pro	Pro Glu Gly Asp	Ser		
	545				555
Glu Thr Lys Ala Pro	Glu Glu Ser Ser Glu	Asp Val Thr Lys	Tyr		
	560				570

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Gln Glu Gly Val Ser Ala Glu Asn Pro Val Glu Asn His Ile Asn
 575 580
 Ile Thr Gln Ser Asp Lys Phe Thr Ala Lys Pro Leu Asp Ser Asn
 590 595
 Ser Gly Glu Arg Asn Asp Leu Asn Leu Asp Arg Ser Cys Gly Val
 605 610
 Pro Glu Glu Ser Ala Ser Ser Glu Lys Ala Lys Glu Pro Glu Thr
 620 625
 Ser Asp Gln Thr Ser Thr Glu Ser Ala Thr Asn Glu Asn Asn Thr
 635 640
 Asn Pro Glu Pro Gln Phe Gln Thr Glu Ala Thr Gly Pro Ser Ala
 650 655
 His Glu Glu Thr Ser Thr Arg Asp Ser Ala Leu Gln Asp Thr Asp
 665 670
 Asp Ser Asp Asp Asp Pro Val Leu Ile Pro Gly Ala Arg Tyr Arg
 680 685
 Ala Gly Pro Gly Asp Arg Arg Ser Ala Val Ala Arg Ile Gln Glu
 695 700
 Phe Phe Arg Arg Arg Lys Glu Arg Lys Glu Met Glu Glu Leu Asp
 710 715
 Thr Leu Asn Ile Arg Arg Pro Leu Val Lys Met Val Tyr Lys Gly
 725 730
 His Arg Asn Ser Arg Thr Met Ile Lys Glu Ala Asn Phe Trp Gly
 740 745
 Ala Asn Phe Val Met Ser Gly Ser Asp Cys Gly His Ile Phe Ile
 755 760
 Trp Asp Arg His Thr Ala Glu His Leu Met Leu Leu Glu Ala Asp
 770 775
 Asn His Val Val Asn Cys Leu Gln Pro His Pro Phe Asp Pro Ile
 785 790
 Leu Ala Ser Ser Gly Ile Asp Tyr Asp Ile Lys Ile Trp Ser Pro
 800 805
 Leu Glu Glu Ser Arg Ile Phe Asn Arg Lys Leu Ala Asp Glu Val
 815 820
 Ile Thr Arg Asn Glu Leu Met Leu Glu Glu Thr Arg Asn Thr Ile
 830 835
 Thr Val Pro Ala Ser Phe Met Leu Arg Met Leu Ala Ser Leu Asn
 845 850
 His Ile Arg Ala Asp Arg Leu Glu Gly Asp Arg Ser Glu Gly Ser
 860 865
 Gly Gln Glu Asn Glu Asn Glu Asp Glu Glu
 875 880

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<211> 855

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5992432CD1

<400> 54

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 20 25 30
 Asn Gln Phe Ser Val Lys Cys Trp Leu Arg Tyr Ile Glu Phe Lys
 35 40 45
 Gln Gly Ala Pro Lys Pro Arg Leu Asn Gln Leu Tyr Glu Arg Ala
 50 55 60
 Leu Lys Leu Leu Pro Cys Ser Tyr Lys Leu Trp Tyr Arg Tyr Leu
 65 70 75
 Lys Ala Arg Arg Ala Gln Val Lys His Arg Cys Val Thr Asp Pro

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	80		85		90
Ala Tyr Glu Asp	Val Asn Asn Cys His	Glu Arg Ala Phe Val	Phe		
95	100	105			
Met His Lys Met	Pro Arg Leu Trp Leu	Asp Tyr Cys Gln Phe	Leu		
110	115	120			
Met Asp Gln Gly	Arg Val Thr His Thr	Arg Arg Thr Phe Asp	Arg		
125	130	135			
Ala Leu Arg Ala	Leu Pro Ile Thr Gln	His Ser Arg Ile Trp	Pro		
140	145	150			
Leu Tyr Leu Arg	Phe Leu Arg Ser His	Pro Leu Pro Glu Thr	Ala		
155	160	165			
Val Arg Gly Tyr	Arg Arg Phe Leu Lys	Leu Ser Pro Glu Ser	Ala		
170	175	180			
Glu Glu Tyr Ile	Glu Tyr Leu Lys Ser	Ser Asp Arg Leu Asp	Glu		
185	190	195			
Ala Ala Gln Arg	Leu Ala Thr Val Val	Asn Asp Glu Arg Phe	Val		
200	205	210			
Ser Lys Ala Gly	Lys Ser Asn Tyr Gln	Leu Trp His Glu Leu	Cys		
215	220	225			
Asp Leu Ile Ser	Gln Asn Pro Asp Lys	Val Gln Ser Leu Asn	Val		
230	235	240			
Asp Ala Ile Ile	Arg Gly Gly Leu Thr	Arg Phe Thr Asp Gln	Leu		
245	250	255			
Gly Lys Leu Trp	Cys Ser Leu Ala Asp	Tyr Tyr Ile Arg Ser	Gly		
260	265	270			
His Phe Glu Lys	Ala Arg Asp Val Tyr	Glu Glu Ala Ile Arg	Thr		
275	280	285			
Val Met Thr Val	Arg Asp Phe Thr Gln	Val Phe Asp Ser Tyr	Ala		
290	295	300			
Gln Phe Glu Glu	Ser Met Ile Ala Ala	Lys Met Glu Thr Ala	Ser		
305	310	315			
Glu Leu Gly Arg	Glu Glu Glu Asp Asp	Val Asp Leu Glu Leu	Arg		
320	325	330			
Leu Ala Arg Phe	Glu Gln Leu Ile Ser	Arg Arg Pro Leu Leu	Leu		
335	340	345			
Asn Ser Val Leu	Leu Arg Gln Asn Pro	His His Val His Glu	Trp		
350	355	360			
His Lys Arg Val	Ala Leu His Gln Gly	Arg Pro Arg Glu Ile	Ile		
365	370	375			
Asn Thr Tyr Thr	Glu Ala Val Gln Thr	Val Asp Pro Phe Lys	Ala		
380	385	390			
Thr Gly Lys Pro	His Thr Leu Trp Val	Ala Phe Ala Lys Phe	Tyr		
395	400	405			
Glu Asp Asn Gly	Gln Leu Asp Asp Ala	Arg Val Ile Leu Glu	Lys		
410	415	420			
Ala Thr Lys Val	Asn Phe Lys Gln Val	Asp Asp Leu Ala Ser	Val		
425	430	435			
Trp Cys Gln Cys	Gly Glu Leu Glu Leu	Arg His Glu Asn Tyr	Asp		
440	445	450			
Glu Ala Leu Arg	Leu Leu Arg Lys Ala	Thr Ala Leu Pro Ala	Arg		
455	460	465			
Arg Ala Glu Tyr	Phe Asp Gly Ser Glu	Pro Val Gln Asn Arg	Val		
470	475	480			
Tyr Lys Ser Leu	Lys Val Trp Ser Met	Leu Ala Asp Leu Glu	Glu		
485	490	495			
Ser Leu Gly Thr	Phe Gln Ser Thr Lys	Ala Val Tyr Asp Arg	Ile		
500	505	510			
Leu Asp Leu Arg	Ile Ala Thr Pro Gln	Ile Val Ile Asn Tyr	Ala		
515	520	525			
Met Phe Leu Glu	Glu His Lys Tyr Phe	Glu Glu Ser Phe Lys	Ala		
530	535	540			
Tyr Glu Arg Gly	Ile Ser Leu Phe Lys	Trp Pro Asn Val Ser	Asp		
545	550	555			

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Ile	Trp	Ser	Thr	Tyr	Leu	Thr	Lys	Phe	Ile	Ala	Arg	Tyr	Gly	Gly
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Arg	Lys	Leu	Glu	Arg	Ala	Arg	Asp	Leu	Phe	Glu	Gln	Ala	Leu	Asp
				575					580					585
Gly	Cys	Pro	Pro	Lys	Tyr	Ala	Lys	Thr	Leu	Tyr	Leu	Leu	Tyr	Ala
				590					595					600
Gln	Leu	Glu	Glu	Glu	Trp	Gly	Leu	Ala	Arg	His	Ala	Met	Ala	Val
				605					610					615
Tyr	Glu	Arg	Ala	Thr	Arg	Ala	Val	Glu	Pro	Ala	Gln	Gln	Tyr	Asp
				620					625					630
Met	Phe	Asn	Ile	Tyr	Ile	Lys	Arg	Ala	Ala	Glu	Ile	Tyr	Gly	Val
				635					640					645
Thr	His	Thr	Arg	Gly	Ile	Tyr	Gln	Lys	Ala	Ile	Glu	Val	Leu	Ser
				650					655					660
Asp	Glu	His	Ala	Arg	Glu	Met	Cys	Leu	Arg	Phe	Ala	Asp	Met	Glu
				665					670					675
Cys	Lys	Leu	Gly	Glu	Ile	Asp	Arg	Ala	Arg	Ala	Ile	Tyr	Ser	Phe
				680					685					690
Cys	Ser	Gln	Ile	Cys	Asp	Pro	Arg	Thr	Thr	Gly	Ala	Phe	Trp	Gln
				695					700					705
Thr	Trp	Lys	Asp	Phe	Glu	Val	Arg	His	Gly	Asn	Glu	Asp	Thr	Ile
				710					715					720
Lys	Glu	Met	Leu	Arg	Ile	Arg	Arg	Ser	Val	Gln	Ala	Thr	Tyr	Asn
				725					730					735
Thr	Gln	Val	Asn	Phe	Met	Ala	Ser	Gln	Met	Leu	Lys	Val	Ser	Gly
				740					745					750
Ser	Ala	Thr	Gly	Thr	Val	Ser	Asp	Leu	Ala	Pro	Gly	Gln	Ser	Gly
				755					760					765
Met	Asp	Asp	Met	Lys	Leu	Leu	Glu	Gln	Arg	Ala	Glu	Gln	Leu	Ala
				770					775					780
Ala	Glu	Ala	Glu	Arg	Asp	Gln	Pro	Leu	Arg	Ala	Gln	Ser	Lys	Ile
				785					790					795
Leu	Phe	Val	Arg	Ser	Asp	Ala	Ser	Arg	Glu	Glu	Leu	Ala	Glu	Leu
				800					805					810
Ala	Gln	Gln	Val	Asn	Pro	Glu	Glu	Ile	Gln	Leu	Gly	Glu	Asp	Glu
				815					820					825
Asp	Glu	Asp	Glu	Met	Asp	Leu	Glu	Pro	Asn	Glu	Val	Arg	Leu	Glu
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<211> 1598

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 116462CB1

<400> 55

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tgcaatccat tggcggtagg aaccacgatt ccggcattc ccagtcttc gactccttcg 180
ggcttccctt tcgggtcttc gaggctgctg aaaccgaaac cgctgtgctg tggcgcgagc 240
gccgagattg attcaccttc acctgtgctg cactccagct gaccgaagta ggaagccaga 300
cgagctgtaa aacatgaacg gaagagtggg ttatttggtc actgaggaag agataaattc 360
taccagaggg cctcagggc tgggcttcaa catgctcggg gggacagatc agcagtatgt 420
ctccaaagac agtggtcatc acgtcagccg catcaagaaa aatggggctg cggcccttga 480
tggcgcgctc caggagggtg ataagatcct ttgcgttaaa ggcgaagacc taagaacctt 540
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cgagcacagg ttacaggtgc agaattggacc tataggacat cgagctgaag gggagcccaag 660
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ggcttttcag agataccggc aacaactttg aaaaacttgc tctctttcaa tactcccaat 780
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catagccaga tttgaagtga ctgataccca ccccaaacct tgctgtttac agtctccaat 900
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ggcttagaac aaatgaggag ttatatattt tactaggact ttgtatagaa attcagctac 1020
aacccaaga gagaagaatt gagtcttctt gtcaccatag gcaatacctt ttttcttagc 1080
tggtcatgca taaaggccag ctatgtgata tttagaggag aaaggatttt tctttttaat 1140
gatcttctct ggggaattat tttggccttt atttaatttc taactacgta cctgggtgac 1200
tatatcgaca aagagttaga agagcatttt tactttttta aaaaagcaaa tacatataa 1260
cacatcagta tgcgaattat atagtataat agtgatccct atggagaatt aaaggtgaga 1320
aagctacttt gtggtgtcta ggtttctgat aaaaggggat atcttaactg aagaatttaa 1380
agagatactt aaacagagca aatgtagtag gaacaaggga gtgagcctta taagaggagc 1440
ttcagttcca ttattaaaa taataactga gactgggaga ggtggcctat gcctgtaaat 1500
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<210> 56
<211> 1432
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1210462CB1

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ctgacccagg tgaaaacaaa atcagagggg aagcttgcga aacagatttg caaagttgtg 180
ttggatcatt ttgaaaaaca gattcccaaa gaactcggag atgcctggaa tacagttaag 240
gagatactaa catctccatc atgtctggca tatgctgtcc tgcttaaccc attcaattat 300
ccttttgaac tggaaaaggga ttacattttg aaggcctatc acacactctc tcagggtatc 360
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ctccagtggt tggctctgga attaagggat ggggagaagg ttctggatct ctgtgtgtct 540
cctggaggga aatcaatagg tctgtctcag tgtgtctgtc caggttatct tcattgtaat 600
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cctttgataa atgtaattaa agtgtctgaa ttggatggca gaaaatggg agatgcacag 720
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gcctggggcc caatgtatgt agccaaattg aagaaatcat ggagcacagg aaaaattggt 1140
catgaatttg taaactgtgt ttatgtgtta ttatatttat atttctgaac tcagtacagt 1200
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<210> 57
<211> 2317
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 1305252CB1

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tgaattctctt atgaaatgcaa agaaaaataa acctgagtgagg ggggaagagc aaatggcctc 300
catcaaaaaa gactactata aagcttttga agatgcagat gagaagggttc agttggcaca 360
ccagatatat gacttggtag atcgacacct gagaaagctg gatcaggaac tggctaaagt 420
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ggaattagac actccttcac agccagtgaa caatcaccat gctcatcac atactccagt 540
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cccaaatgtg ttattttttt ttggtgcca agtaaacctt taaaaaatgt gccaatgtga 2160
attaaggggg gttaaaaaata aaaggttttt ttaaaaaaaa tttaaaacaa acaaaaaaga 2220
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<210> 58

<211> 1774

<212> DNA

<213> Homo sapiens

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<221> misc_feature

<223> Incyte ID No: 1416289CB1

<400> 58

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ttcaggtgccc ttgaatggct tctaaacaat ttgatgactc accgaatagt tgaactttt 180
aaagaactca gtataaagt catgaacacg ctcaattggt ctactaaact atttggtagt 240
caagttggaga tggatatata cactgtctca aaaaagtgga tgttctctca acttgcgctc 300
tcttggaaat gatctttaa acagcttttg acagaacacg atgtctggtt tcttaaacag 360
aggaagaagt ttgaaggtat ggcctttctt gaaactgaac aagaaaaacc atttggtyca 420
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gaacaagatg ctgtatgacc ttcaaatggt gtaggagctc aagaatacaa taagaagaa 600
gctatgctgc gggcagaaga ggaacagtga gtggggccct aagaatgtga atactgctg 660
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cgttggagac gtttttaact cggtctcgac ctacttgtaa ctacaccaa tgcatactc 780
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aggagatcat cctttagatt acgtttggct tcttttgata gtagtggaaa actaatgtg 900
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tcactcagtg	gaaacagtag	cacttttgaaa	acttttttagg	ccagcttttaa	tttaaatggcc	1080
ctctgatata	tcacatcgaa	ggtagactaac	aatgacaaag	gccttatgaa	ctgtacagac	1140
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<223> Incyte ID No: 1887228CB1

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<213> Homo sapiens

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<223> Incyte ID No: 3215187CB1

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<213> Homo sapiens

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<212> DNA

<213> Homo sapiens

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<211> 1541

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<221> misc_feature

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<400> 82

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<213> Homo sapiens

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<211> 868

<212> DNA

<213> Homo sapiens

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<223> Incyte ID No: 1620092CB1

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<213> Homo sapiens

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<211> 2031

<212> DNA

<213> Homo sapiens

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<221> misc_feature

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<211> 2070

<212> DNA

<213> Homo sapiens

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<223> Incyte ID No: 2668536CB1

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<221> unsure

<222> 2058, 2067

<223> a, t, c, g, or other

<400> 95

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<210> 96

<211> 2046

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2683225CB1

<400> 96

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<213> Homo sapiens

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<223> Incyte ID No: 2959521CB1

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DECLARATION AND POWER OF ATTORNEY FOR
UNITED STATES PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name, and

I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if more than one name is listed below) of the subject matter which is claimed and for which a United States patent is sought on the invention entitled

CELL CYCLE AND CELL PROLIFERATION PROTEINS

the specification of which:

 / is attached hereto.

 / was filed on _____ as application Serial No. _____ and if this box contains an X /, was amended on _____.

 / X / was filed as Patent Cooperation Treaty international application No. PCT/US00/19948 on July 21, 2000, if this box contains an X /, was amended on under Patent Cooperation Treaty Article 19 on _____ 2001, and if this box contains an X /, was amended on _____.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge my duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim the benefit under Title 35, United States Code, §119 or §365(a)-(b) of any foreign application(s) for patent or inventor's certificate indicated below and of any Patent Cooperation Treaty international applications(s) designating at least one country other than the United States indicated below and have also identified below any foreign application(s) for patent or inventor's certificate and Patent Cooperation Treaty international application(s) designating at least one country other than the United States for the same subject matter and having a filing date before that of the application for said subject matter the priority of which is claimed:

Docket No.: PF-0722 USN

Country	Number	Filing Date	Priority Claimed
_____	_____	_____	/ / Yes / / No
_____	_____	_____	/ / Yes / / No

I hereby claim the benefit under Title 35, United States Code, §119(c) of any United States provisional application(s) listed below.

Application Serial No.	Filed	Status (Pending, Abandoned, Patented)
60/145,075	July 21, 1999	Expired
60/153,129	September 8, 1999	Expired
60/164,647	November 10, 1999	Expired

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in said prior application(s) in the manner required by the first paragraph of Title 35, United States Code §112, I acknowledge my duty to disclose material information as defined in Title 37 Code of Federal Regulations, §1.56(a) which occurred between the filing date(s) of the prior application(s) and the national or Patent Cooperation Treaty international filing date of this application:

Application Serial No.	Filed	Status (Pending, Abandoned, Patented)
_____	_____	_____

I hereby appoint the following:

Lucy J. Billings	Reg. No. <u>36,749</u>
Michael C. Cerrone	Reg. No. <u>39,132</u>
Diana Hamlet-Cox	Reg. No. <u>33,302</u>
Richard C. Ekstrom	Reg. No. <u>37,027</u>
Barrie D. Greene	Reg. No. <u>46,740</u>
Lynn E. Murry	Reg. No. <u>42,918</u>
Shirley A. Recipon	Reg. No. <u>47,016</u>
Susan K. Sather	Reg. No. <u>44,316</u>
Michelle M. Stempien	Reg. No. <u>41,327</u>
David G. Streeter	Reg. No. <u>43,168</u>
Stephen Todd	Reg. No. <u>47,139</u>
P. Ben Wang	Reg. No. <u>41,420</u>

respectively and individually, as my patent attorneys and/or agents, with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith. Please address all communications to:

Docket No.: PF-0722 USN

LEGAL DEPARTMENT
INCYTE GENOMICS, INC.
3160 PORTER DRIVE, PALO ALTO, CA 94304

TEL: 650-855-0555 FAX: 650-849-8886 or 650-845-4166

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

First Joint Inventor:

100

Full name: Jennifer L. Hillman
 Signature: *Jennifer L. Hillman*
 Date: September 21, 2001
 Citizenship: United States
 Residence: Mountain View, California *CA*
 P.O. Address: 230 Monroe Drive, #17
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Second Joint Inventor:

200

Full name: Preeti Lal
 Signature: *Preeti Lal*
 Date: September 10, 2001
 Citizenship: India
 Residence: Santa Clara, California *CA*
 P.O. Address: P.O. Box 5142
Santa Clara, California 95056

Docket No.: PF-0722 USN

LEGAL DEPARTMENT
INCYTE GENOMICS, INC.
3160 PORTER DRIVE, PALO ALTO, CA 94304

TEL: 650-855-0555 FAX: 650-849-8886 or 650-845-4166

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

First Joint Inventor:

Full name: Jennifer L. Hillman
Signature: _____
Date: _____, 2001
Citizenship: United States
Residence: Mountain View, California
P.O. Address: 230 Monroe Drive, #17
Mountain View, California 94040

Second Joint Inventor:

Full name: Preeti Lal
Signature: _____
Date: _____, 2001
Citizenship: India
Residence: Santa Clara, California
P.O. Address: P.O. Box 5142
Santa Clara, California 95056

Docket No.: PF-0722 USN**Third Joint Inventor:**Full name: Y. Tom Tang

Signature: _____

Date: _____, 2001

Citizenship: United StatesResidence: San Jose, CaliforniaP.O. Address: 4230 Ranwick Court
San Jose, California 95118**Fourth Joint Inventor:**Full name: Henry Yue

Signature: _____

Date: _____, 2001

Citizenship: United StatesResidence: Sunnyvale, CaliforniaP.O. Address: 826 Lois Avenue
Sunnyvale, California 94087**Fifth Joint Inventor:**Full name: Janice Au-Young

Signature: _____

Date: _____, 2001

Citizenship: United StatesResidence: Brisbane, CaliforniaP.O. Address: 233 Golden Eagle Lane
Brisbane, California 94005

Docket No.: PF-0722 USN

Sixth Joint Inventor:

Full name: Olga Bandman
Signature: _____
Date: _____, 2001
Citizenship: United States
Residence: Mountain View, California
P.O. Address: 366 Anna Avenue
Mountain View, California 94043

Seventh Joint Inventor:

Full name: Yalda Azimzai
Signature: _____
Date: _____, 2001
Citizenship: United States
Residence: Castro Valley, California
P.O. Address: 5518 Boulder Canyon Drive
Castro Valley, California 94552

Eighth Joint Inventor:

Full name: Junming Yang
Signature: _____
Date: _____, 2001
Citizenship: China
Residence: San Jose, California
P.O. Address: 7125 Bark Lane
San Jose, California 95129

Docket No.: PF-0722 USN**Ninth Joint Inventor:**Full name: Dyung Aina M. Lu

Signature: _____

Date: _____, 2001

Citizenship: United StatesResidence: San Jose, CaliforniaP.O. Address: 233 Coy Drive
San Jose, California 95123**Tenth Joint Inventor:**Full name: Mariah R. Baughn

Signature: _____

Date: _____, 2001

Citizenship: United StatesResidence: San Leandro, CaliforniaP.O. Address: 14244 Santiago Road
San Leandro, California 94577**Eleventh Joint Inventor:**Full name: Chandra Patterson

Signature: _____

Date: _____, 2001

Citizenship: United StatesResidence: Menlo Park, CaliforniaP.O. Address: 490 Sherwood Way, #1
Menlo Park, California 94025

Docket No.: PF-0722 USN

Third Joint Inventor:

300

Full name: Y. Tom Tang
 Signature: *Y. Tom Tang*
 Date: September 10, 2001
 Citizenship: United States
 Residence: San Jose, California
 P.O. Address: 4230 Ranwick Court
San Jose, California 95118

Fourth Joint Inventor:

400

Full name: Henry Yue
 Signature: *Henry Yue*
 Date: September 24, 2001
 Citizenship: United States
 Residence: Sunnyvale, California
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Fifth Joint Inventor:

500

Full name: Janice Au-Young
 Signature: *Janice Au-Young*
 Date: September 7, 2001
 Citizenship: United States
 Residence: Brisbane, California
 P.O. Address: 233 Golden Eagle Lane
Brisbane, California 94005

Docket No.: PF-0722 USN

Sixth Joint Inventor:

600

Full name: Olga Bandman
 Signature: Olga Bandman
 Date: 12 September, 2001
 Citizenship: United States
 Residence: Mountain View, California ^{CA}
 P.O. Address: 366 Anna Avenue
Mountain View, California 94043

Seventh Joint Inventor:

700

Full name: Yalda Azimzai
 Signature: Yalda Azimzai
 Date: September 13, 2001
 Citizenship: United States
 Residence: Castro Valley, California ^{CA}
 P.O. Address: 5518 Boulder Canyon Drive
Castro Valley, California 94552

Eighth Joint Inventor:

800

Full name: Junming Yang
 Signature: Junming Yang
 Date: September 17, 2001
 Citizenship: China
 Residence: San Jose, California ^{CA}
 P.O. Address: 7125 Bark Lane
San Jose, California 95129

Ninth Joint Inventor:

900

Full name: Dyung Aina M. Lu
 Signature: [Signature]
 Date: Sept 7, 2001
 Citizenship: United States
 Residence: San Jose, California
 P.O. Address: 233 Coy Drive
San Jose, California 95123

Tenth Joint Inventor:

1000

RECEIVED
 10 JUL 2002
 Legal Staff
 International Division

Full name: Mariah R. Baughn
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 Citizenship: United States
 Residence: San Leandro, California
 P.O. Address: 14244 Santiago Road
San Leandro, California 94577

Eleventh Joint Inventor:

1100

Full name: Chandra Patterson AW124 CA 9/10/01
 Signature: Chandra Awign
 Date: September 10, 2001
 Citizenship: United States
 Residence: Menlo Park, California
 P.O. Address: 490 Sherwood Way, #1
Menlo Park, California 94025

Docket No.: PF-0722 USN

Twelfth Joint Inventor:

1200

Full name:

Purvi Shah

Signature:

Purvi Shah

Date:

Sept. 20, 2001

Citizenship:

India

Residence:

San Jose, California

P.O. Address:

859 Salt Lake Drive
San Jose, California 95133

Docket No.: PF-0722 USN

Twelfth Joint Inventor:

Full name: Purvi Shah

Signature: _____

Date: _____, 2001

Citizenship: India

Residence: San Jose, California

P.O. Address: 859 Salt Lake Drive
San Jose, California 95133

Docket No.: PF-0722 USN

Country	Number	Filing Date	Priority Claimed
_____	_____	_____	<input type="checkbox"/> Yes <input type="checkbox"/> No
_____	_____	_____	<input type="checkbox"/> Yes <input type="checkbox"/> No

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below.

Application Serial No.	Filed	Status (Pending, Abandoned, Patented)
60/145,075	July 21, 1999	Expired
60/153,129	September 8, 1999	Expired
60/164,647	November 10, 1999	Expired

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in said prior application(s) in the manner required by the first paragraph of Title 35, United States Code §112, I acknowledge my duty to disclose material information as defined in Title 37 Code of Federal Regulations, §1.56(a) which occurred between the filing date(s) of the prior application(s) and the national or Patent Cooperation Treaty international filing date of this application:

Application Serial No.	Filed	Status (Pending, Abandoned, Patented)
_____	_____	_____

I hereby appoint the following:

Lucy J. Billings	Reg. No. 36,749
Michael C. Cerrone	Reg. No. 39,132
Diana Hamlet-Cox	Reg. No. 33,302
Richard C. Ekstrom	Reg. No. 37,027
Barrie D. Greene	Reg. No. 46,740
Lynn E. Murry	Reg. No. 42,918
Shirley A. Recipon	Reg. No. 47,016
Susan K. Sather	Reg. No. 44,316
Michelle M. Stempien	Reg. No. 41,327
David G. Streeter	Reg. No. 43,168
Stephen Todd	Reg. No. 47,139
P. Ben Wang	Reg. No. 41,420

respectively and individually, as my patent attorneys and/or agents, with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith. Please address all communications to:

Docket No.: PF-0722 USN

**DECLARATION AND POWER OF ATTORNEY FOR
UNITED STATES PATENT APPLICATION**

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name, and

I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if more than one name is listed below) of the subject matter which is claimed and for which a United States patent is sought on the invention entitled

CELL CYCLE AND CELL PROLIFERATION PROTEINS

the specification of which:

 is attached hereto.

 was filed on _____ as application Serial No. _____ and if this box contains an X , was amended on _____.

 X was filed as Patent Cooperation Treaty international application No. PCT/US00/19948 on July 21, 2000, if this box contains an X , was amended on under Patent Cooperation Treaty Article 19 on _____ 2001, and if this box contains an X , was amended on _____.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge my duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim the benefit under Title 35, United States Code, §119 or §365(a)-(b) of any foreign application(s) for patent or inventor's certificate indicated below and of any Patent Cooperation Treaty international applications(s) designating at least one country other than the United States indicated below and have also identified below any foreign application(s) for patent or inventor's certificate and Patent Cooperation Treaty international application(s) designating at least one country other than the United States for the same subject matter and having a filing date before that of the application for said subject matter the priority of which is claimed:

SEQUENCE LISTING

<110> INCYTE GENOMICS, INC.
HILLMAN, Jennifer L.
LAL, Preeti
TANG, Y. Tom
YUE, Henry
AU-YOUNG, Janice
BANDMAN, Olga
AZIMZAI, Yalda
YANG, Junming
LU, Dyung Aina M.
BAUGHN, Mariah R.
PATTERSON, Chandra
SHAH, Purvi

<120> CELL CYCLE AND PROLIFERATION PROTEINS

<130> PF-0722 PCT

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<150> 60/145,075; 60/153,129; 60/164,647

<151> 1999-07-21; 1999-09-08; 1999-11-10

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				20					25					30
Thr	Asp	Gln	Gln	Tyr	Val	Ser	Asn	Asp	Ser	Gly	Ile	Tyr	Val	Ser
				35					40					45
Arg	Ile	Lys	Glu	Asn	Gly	Ala	Ala	Ala	Leu	Asp	Gly	Arg	Leu	Gln
				50					55					60
Glu	Gly	Asp	Lys	Ile	Leu	Ser	Val	Asn	Gly	Gln	Asp	Leu	Lys	Asn
				65					70					75
Leu	Leu	His	Gln	Asp	Ala	Val	Asp	Leu	Phe	Arg	Asn	Ala	Gly	Tyr
				80					85					90
Ala	Val	Ser	Leu	Arg	Val	Gln	His	Arg	Leu	Gln	Val	Gln	Asn	Gly
				95					100					105
Pro	Ile	Gly	His	Arg	Gly	Glu	Gly	Asp	Pro	Ser	Gly	Ile	Pro	Ile
				110					115					120
Phe	Met	Val	Leu	Val	Pro	Val	Phe	Ala	Leu	Thr	Met	Val	Ala	Ala
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WO 01/07471

PCT/US00/19948

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				20					25					30
Lys	Glu	Leu	Gly	Asp	Ala	Trp	Asn	Thr	Val	Arg	Glu	Ile	Leu	Thr
				35					40					45
Ser	Pro	Ser	Cys	Trp	Gln	Tyr	Ala	Val	Leu	Leu	Asn	Arg	Phe	Asn
				50					55					60
Tyr	Pro	Phe	Glu	Leu	Glu	Lys	Asp	Leu	His	Leu	Lys	Gly	Tyr	His
				65					70					75
Thr	Leu	Ser	Gln	Gly	Ser	Leu	Pro	Asn	Tyr	Pro	Lys	Ser	Val	Lys
				80					85					90
Cys	Tyr	Leu	Ser	Arg	Thr	Pro	Gly	Arg	Ile	Pro	Ser	Glu	Arg	His
				95					100					105
Gln	Ile	Gly	Asn	Leu	Lys	Lys	Tyr	Tyr	Leu	Leu	Asn	Ala	Ala	Ser
				110					115					120
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				125					130					135
Leu	Asp	Leu	Cys	Ala	Ala	Pro	Gly	Gly	Lys	Ser	Ile	Ala	Leu	Leu
				140					145					150
Gln	Cys	Ala	Cys	Pro	Gly	Tyr	Leu	His	Cys	Asn	Glu	Tyr	Asp	Ser
				155					160					165
Leu	Arg	Leu	Arg	Trp	Leu	Arg	Gln	Thr	Leu	Glu	Ser	Phe	Ile	Pro
				170					175					180
Gln	Pro	Leu	Ile	Asn	Val	Ile	Lys	Val	Ser	Glu	Leu	Asp	Gly	Arg
				185					190					195
Lys	Met	Gly	Asp	Ala	Gln	Pro	Glu	Met	Phe	Asp	Lys	Val	Leu	Val
				200					205					210
Asp	Ala	Pro	Cys	Ser	Asn	Asp	Arg	Ser	Trp	Leu	Phe	Ser	Ser	Asp
				215					220					225
Ser	Gln	Lys	Ala	Ser	Cys	Arg	Ile	Ser	Gln	Arg	Arg	Asn	Leu	Pro
				230					235					240
Leu	Leu	Gln	Ile	Glu	Leu	Leu	Arg	Ser	Ala	Ile	Lys	Ala	Leu	Arg
				245					250					255
Pro	Gly	Gly	Ile	Leu	Val	Tyr	Ser	Thr	Cys	Thr	Leu	Ser	Lys	Ala
				260					265					270
Glu	Asn	Gln	Asp	Val	Ile	Ser	Glu	Ile	Leu	Asn	Ser	His	Gly	Asn
				275					280					285
Ile	Met	Pro	Met	Asp	Ile	Lys	Gly	Ile	Ala	Arg	Thr	Cys	Ser	His
				290					295					300
Asp	Phe	Thr	Phe	Ala	Pro	Thr	Gly	Gln	Glu	Cys	Gly	Leu	Leu	Val
				305					310					315
Ile	Pro	Asp	Lys	Gly	Lys	Ala	Trp	Gly	Pro	Met	Tyr	Val	Ala	Lys
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WO 01/07471

PCT/US00/19948

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35     40     45
Phe Phe Met Asn Ala Lys Lys Asn Lys Pro Glu Trp Arg Glu Glu
50     55     60
Gln Met Ala Ser Ile Lys Lys Asp Tyr Tyr Lys Ala Leu Glu Asp
65     70     75
Ala Asp Glu Lys Val Gln Leu Ala Asn Gln Ile Tyr Asp Leu Val
80     85     90
Asp Arg His Leu Arg Lys Leu Asp Gln Glu Leu Ala Lys Phe Lys
95     100    105
Met Glu Leu Glu Ala Asp Asn Ala Gly Ile Thr Glu Ile Leu Glu
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Arg Arg Ser Leu Glu Leu Asp Thr Pro Ser Gln Pro Val Asn Asn
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His His Ala His Ser His Thr Pro Val Glu Lys Arg Lys Tyr Asn
140    145    150
Pro Thr Ser His His Thr Thr Thr Asp His Ile Pro Glu Lys Lys
155    160    165
Phe Lys Ser Glu Ala Leu Leu Ser Thr Leu Thr Ser Asp Ala Ser
170    175    180
Lys Glu Asn Thr Leu Gly Cys Arg Asn Asn Asn Ser Thr Ala Ser
185    190    195
Ser Asn Asn Ala Tyr Asn Val Asn Ser Ser Gln Pro Leu Gly Ser
200    205    210
Tyr Asn Ile Gly Ser Leu Ser Ser Gly Thr Gly Ala Gly Ala Ile
215    220    225
Thr Met Ala Ala Ala Gln Ala Val Gln Ala Thr Ala Gln Met Lys
230    235    240
Glu Gly Arg Arg Thr Ser Ser Leu Lys Ala Ser Tyr Glu Ala Phe
245    250    255
Lys Asn Asn Asp Phe Gln Leu Gly Lys Glu Phe Ser Met Ala Arg
260    265    270
Glu Thr Val Gly Tyr Ser Ser Ser Ser Ala Leu Met Thr Thr Leu
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Thr Gln Asn Ala Ser Ser Ser Ala Ala Asp Ser Arg Ser Gly Arg
290    295    300
Lys Ser Lys Asn Asn Asn Lys Ser Ser Ser Gln Gln Ser Ser Ser
305    310    315
Ser Ser Ser Ser Ser Ser Leu Ser Ser Cys Ser Ser Ser Ser Thr
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Val Val Gln Glu Ile Ser Gln Gln Thr Thr Val Val Pro Glu Ser
335    340    345
Asp Ser Asn Ser Gln Val Asp Trp Thr Tyr Asp Pro Asn Glu Pro
350    355    360
Arg Tyr Cys Ile Cys Asn Gln Val Ser Tyr Gly Glu Met Val Gly
365    370    375
Cys Asp Asn Gln Asp Cys Pro Ile Glu Trp Phe His Tyr Gly Cys
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WO 01/07471

PCT/US00/19948

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Phe Lys Glu Leu Ser Ile Asn Val Met Lys Gln Leu Ile Gly Ser
35     40     45
Ser Asn Leu Phe Val Met Gln Val Glu Met Asp Ile Tyr Thr Ala
50     55     60
Leu Lys Lys Trp Met Phe Leu Gln Leu Val Pro Ser Trp Asn Gly
65     70     75
Ser Leu Lys Gln Leu Leu Thr Glu Thr Asp Val Trp Phe Ser Lys
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Gln Arg Lys Asp Phe Glu Gly Met Ala Phe Leu Glu Thr Glu Gln
95     100    105
Gly Lys Pro Phe Val Ser Val Phe Arg His Leu Arg Leu Gln Tyr
110    115    120
Ile Ile Ser Asp Leu Ala Ser Ala Arg Ile Ile Glu Gln Asp Ala
125    130    135
Val Val Pro Ser Glu Trp Leu Ser Ser Val Tyr Lys Gln Gln Trp
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Phe Ala Met Leu Arg Ala Glu Gln Asp Ser Glu Val Gly Pro Gln
155    160    165
Glu Ile Asn Lys Glu Glu Leu Glu Gly Asn Ser Met Arg Cys Gly
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Arg Lys Leu Ala Lys Asp Gly Glu Tyr Cys Trp Arg Trp Thr Gly
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Ile Ile Phe Lys Arg Asn Thr Leu Asn Gln Pro Cys Ser Gly Ser
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Val Ser Leu Gln Pro Arg Arg Ser Ile Ala Phe Arg Leu Arg Leu
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Ala Ser Phe Asp Ser Ser Gly Lys Leu Ile Cys Ser Arg Thr Thr
245    250    255
Gly Tyr Gln Ile Leu Thr Leu Glu Lys Asp Gln Glu Gln Val Val
260    265    270
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35     40     45
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50     55     60
Lys Asp Leu Ile Lys Val Ala Ile Lys Val Ala Val Leu His Arg
65     70     75

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PCT/US00/19948

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 Glu Val Asp Phe Thr Phe Glu Ala Ala Val Leu Ala Gly Leu Leu
 110 115 120
 Thr Glu Cys Arg Asp Val Leu Leu Glu Leu Val Glu His His Leu
 125 130 135
 Thr Pro Lys Ser His Gly Arg Ile Arg His Val Phe Asp His Phe
 140 145 150
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 Gln His Leu Gly Lys Ile Cys Asp Gly Leu Arg Lys Leu Leu Asp
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 20 25 30
 Cys Cys Cys Cys Arg Ala Lys Phe Pro Leu Phe Ser Trp Pro Pro
 35 40 45
 Ser Cys Leu Phe Cys Lys Arg Ala Val Cys Thr Ser Cys Ser Ile
 50 55 60
 Lys Met Lys Met Pro Ser Lys Lys Phe Gly His Ile Pro Val Tyr
 65 70 75
 Thr Leu Gly Phe Glu Ser Pro Gln Arg Val Ser Ala Ala Lys Thr
 80 85 90
 Ala Pro Ile Gln Arg Arg Asp Ile Phe Gln Ser Leu Gln Gly Pro
 95 100 105
 Gln Trp Gln Ser Val Glu Glu Ala Phe Pro His Ile Tyr Ser His
 110 115 120
 Gly Cys Val Leu Lys Asp Val Cys Ser Glu Cys Thr Ser Phe Val
 125 130 135
 Ala Asp Val Val Arg Ser Ser Arg Lys Ser Val Asp Val Leu Asn
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<223> Incyte ID No: 1752768CD1

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Met Val Pro Val Ala Val Thr Ala Ala Val Ala Pro Val Leu Ser
 1 5 10 15
 Ile Asn Ser Asp Phe Ser Asp Leu Arg Glu Ile Lys Lys Gln Leu

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Leu Leu Ile Ala	20	Leu Thr Arg Glu	25	Gly Leu Leu His	30
Ser Lys Trp Ser	35	Glu Leu Ala Phe	40	Ser Leu Pro Ala Leu	45
Leu Ala Glu Leu	50	Pro Pro Pro Pro	55	Ile Thr Glu Glu Asp	60
Gln Asp Met Asp	65	Ala Tyr Thr Leu	70	Lys Ala Tyr Phe Asp	75
Lys Glu Tyr Asp	80	Arg Ala Ala His	85	Leu His Gly Cys Asn	90
Lys Lys Ala Tyr	95	Phe Leu Tyr Met	100	Ser Arg Tyr Leu Ser	105
Glu Lys Lys Lys	110	Asp Asp Glu Thr	115	Val Ser Leu Gly Pro	120
Glu Lys Gly Gln	125	Val Lys Asn Glu	130	Ala Leu Arg Val	135
Glu Leu Ser Lys	140	Lys His Gln Ala	145	Glu Asp Gly Phe	150
Leu Tyr Leu Tyr	155	Gly Val Val Leu	160	Arg Leu Val Lys	165
Glu Ala Ile Asp	170	Val Phe Val Glu	175	Thr His Val Leu	180
His Trp Gly Ala	185	Trp Leu Glu Leu	190	Cys Leu Ile Thr	195
Glu Met Leu Lys	200	Phe Leu Ser Leu	205	Pro Asp Thr Trp	210
Phe Phe Leu Ala	215	His Ile Tyr Thr	220	Glu Gln Leu Ile	225
Ala Leu Gln Lys	230	Tyr Gln Asn Leu	235	Ile Asp Val Gly	240
Ser Ser Tyr Ile	245	Val Ser Gln Ile	250	Ala Tyr His Asn	255
Arg Asp Ile Asp	260	Lys Ala Leu Ser	265	Ile Phe Asn Glu	270
Gln Asp Pro Tyr	275	Arg Ile Glu Asn	280	Met Asp Thr Phe	285
Leu Tyr Val Arg	290	Ser Met Lys Ser	295	Glu Ser Tyr Leu	300
Asn Leu Cys Glu	305	Ile Asp Lys Tyr	310	Arg Val Glu Thr	315
Ile Gly Asn Tyr	320	Tyr Ser Leu Arg	325	Ser Gln His Glu	330
Leu Tyr Phe Gln	335	Arg Ala Leu Lys	340	Leu Asn Pro Arg	345
Ala Trp Thr Leu	350	Met Gly His Glu	355	Tyr Met Glu Met	360
Ser Ala Ala Ile	365	Gln Ala Tyr Arg	370	His Ala Ile Glu	375
Arg Asp Tyr Arg	380	Ala Trp Tyr Gly	385	Leu Gln Thr Tyr	390
Leu Lys Met Pro	395	Phe Tyr Cys Leu	400	Tyr Cys Arg Arg	405
Gln Leu Arg Pro	410	Asn Asp Ser Arg	415	Met Leu Val Ala	420
Cys Tyr Glu Lys	425	Leu Asn Gln Leu	430	Val Glu Ala Lys	435
Trp Arg Ala Tyr	440	Ala Val Gly Asp	445	Val Glu Lys Met	450
Lys Leu Ala Lys	455	Leu His Glu Gln	460	Leu Thr Glu Ser	465
Ala Gln Cys Tyr	470	Ile Lys Tyr Ile	475	Gln Asp Ile Tyr	480
	485		490	Ser Cys Gly	495

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Glu Ile Val Glu His Leu Glu Glu Ser Thr Ala Phe Arg Tyr Leu
 500 510
 Ala Gln Tyr Tyr Phe Lys Cys Lys Leu Trp Asp Glu Ala Ser Thr
 515 525
 Cys Ala Gln Lys Cys Cys Ala Phe Asn Asp Thr Arg Glu Glu Gly
 530 540
 Lys Ala Leu Leu Arg Gln Ile Leu Gln Leu Arg Asn Gln Gly Glu
 545 555
 Thr Pro Thr Thr Glu Val Pro Ala Pro Phe Phe Leu Pro Ala Ser
 560 570
 Leu Ser Ala Asn Asn Thr Pro Thr Arg Arg Val Ser Pro Leu Asn
 575 585
 Leu Ser Ser Val Thr Pro
 590

<210> 8

<211> 463

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1887228CD1

<400> 8

Met Pro Leu Leu Asn Trp Val Ala Leu Lys Pro Ser Gln Ile Thr
 1 5 10 15
 Gly Thr Val Phe Thr Glu Leu Asn Asp Glu Lys Val Leu Gln Glu
 20 25 30
 Leu Asp Met Ser Asp Phe Glu Glu Gln Phe Lys Thr Lys Ser Gln
 35 40 45
 Gly Pro Ser Leu Asp Leu Ser Ala Leu Lys Ser Lys Ala Ala Gln
 50 55 60
 Lys Ala Pro Ser Lys Ala Thr Leu Ile Glu Ala Asn Arg Ala Lys
 65 70 75
 Asn Leu Ala Ile Thr Leu Arg Lys Gly Asn Leu Gly Ala Glu Arg
 80 85 90
 Ile Cys Gln Ala Ile Glu Ala Tyr Asp Leu Gln Ala Leu Gly Leu
 95 100 105
 Asp Phe Leu Glu Leu Leu Met Arg Phe Leu Pro Thr Glu Tyr Glu
 110 115 120
 Arg Ser Leu Ile Thr Arg Phe Glu Arg Glu Gln Arg Pro Met Glu
 125 130 135
 Glu Leu Ser Glu Glu Asp Arg Phe Met Leu Cys Phe Ser Arg Ile
 140 145 150
 Pro Arg Leu Pro Glu Arg Met Thr Thr Leu Thr Phe Leu Gly Asn
 155 160 165
 Phe Pro Asp Thr Ala Gln Leu Leu Met Pro Gln Leu Asn Ala Ile
 170 175 180
 Ile Ala Ala Ser Met Ser Ile Lys Ser Ser Asp Lys Leu Arg Gln
 185 190 195
 Ile Leu Glu Ile Val Leu Ala Phe Gly Asn Tyr Met Asn Ser Ser
 200 205 210
 Lys Arg Gly Ala Ala Tyr Gly Phe Arg Leu Gln Ser Leu Asp Ala
 215 220 225
 Leu Leu Glu Met Lys Ser Thr Asp Arg Lys Gln Thr Leu Leu His
 230 235 240
 Tyr Leu Val Lys Val Ile Ala Glu Lys Tyr Pro Gln Leu Thr Gly
 245 250 255
 Phe His Ser Asp Leu His Phe Leu Asp Lys Ala Gly Ser Val Ser
 260 265 270
 Leu Asp Ser Val Leu Ala Asp Val Arg Ser Leu Gln Arg Gly Leu
 275 280 285
 Glu Leu Thr Gln Arg Glu Phe Val Arg Gln Asp Asp Cys Met Val

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290
Leu Lys Glu Phe 300
305 Leu Arg Ala Asn Ser 300
Leu Ala Asp Ser 310
320 Lys Thr Ala Gln Glu 315
335 Glu Tyr Phe Gly 325
340 Asn Pro Lys Thr 330
350 Phe Ser Leu Phe 340
355 Ser Arg Phe Ile Lys 345
365 Gln Glu Val Glu 355
370 Gln Trp Lys Lys Glu 360
380 Gly Ala Asp Thr 370
385 Pro Gly Lys Gly Glu 375
395 Pro Pro Lys Ala 385
400 Arg Arg Pro Gln Met 390
410 Lys Arg Arg Gln 400
415 Gln Lys Glu Pro Leu 405
425 Asp Gly Ala Ile 415
430 Glu Asp Ile Ile Thr 420
440 Tyr Ile Arg Ala 430
445 Asp Thr Gly Arg Ser 435
455 Pro Gly Pro Pro 445
Leu Gln Val Thr Ser 450
Leu Ser Leu 460
460

<210> 9
<211> 270
<212> PRT
<213> Homo sapiens

<220>
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<223> Incyte ID No: 1988468CD1

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Met Ala Asp His Met Met Ala Met Asn His Gly Arg Phe Pro Asp
1 5 10 15
Gly Thr Asn Gly Leu His His His Pro Ala His Arg Met Gly Met
20 25 30
Gly Gln Phe Pro Ser Pro His His His Gln Gln Gln Pro Gln
35 40 45
His Ala Phe Asn Ala Leu Met Gly Glu His Ile His Tyr Gly Ala
50 55 60
Gly Asn Met Asn Ala Thr Ser Gly Ile Arg His Ala Met Gly Pro
65 70 75
Gly Thr Val Asn Gly Gly His Pro Pro Ser Ala Leu Ala Pro Ala
80 85 90
Ala Arg Phe Asn Asn Ser Gln Phe Met Gly Pro Pro Val Ala Ser
95 100 105
Gln Gly Gly Ser Leu Pro Ala Ser Met Gln Leu Gln Lys Leu Asn
110 115 120
Asn Gln Tyr Phe Asn His His Pro Tyr Pro His Asn His Tyr Met
125 130 135
Pro Asp Leu His Pro Ala Ala Gly His Gln Met Asn Gly Thr Asn
140 145 150
Gln His Phe Arg Asp Cys Asn Pro Lys His Ser Gly Gly Ser Ser
155 160 165
Thr Pro Gly Gly Ser Gly Gly Ser Ser Thr Pro Gly Gly Ser Gly
170 175 180
Ser Ser Ser Gly Gly Ala Gly Ser Ser Asn Ser Gly Gly Gly
185 190 195
Ser Gly Ser Gly Asn Met Pro Ala Ser Val Ala His Val Pro Ala
200 205 210
Ala Met Leu Pro Pro Asn Val Ile Asp Thr Asp Phe Ile Asp Glu
215 220 225

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Glu	Val	Leu	Met	Ser	Leu	Val	Ile	Glu	Met	Gly	Leu	Asp	Arg	Ile
				230					235					240
Lys	Glu	Leu	Pro	Glu	Leu	Trp	Leu	Gly	Gln	Asn	Glu	Phe	Asp	Phe
				245					250					255
Met	Thr	Asp	Phe	Val	Cys	Lys	Gln	Gln	Pro	Ser	Arg	Val	Ser	Cys
				260					265					270

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 <211> 255
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2049176CD1

<400> 10

Met	Val	Ser	Trp	Met	Ile	Ser	Arg	Ala	Val	Val	Leu	Val	Phe	Gly
1				5					10					15
Met	Leu	Tyr	Pro	Ala	Tyr	Tyr	Ser	Tyr	Lys	Ala	Val	Lys	Thr	Lys
				20					25					30
Asn	Val	Lys	Glu	Tyr	Val	Arg	Trp	Met	Met	Tyr	Trp	Ile	Val	Phe
				35					40					45
Ala	Leu	Tyr	Thr	Val	Ile	Glu	Thr	Val	Ala	Asp	Gln	Thr	Val	Ala
				50					55					60
Trp	Phe	Pro	Leu	Tyr	Tyr	Glu	Leu	Lys	Ile	Ala	Phe	Val	Ile	Trp
				65					70					75
Leu	Leu	Ser	Pro	Tyr	Thr	Lys	Gly	Ala	Ser	Leu	Ile	Tyr	Arg	Lys
				80					85					90
Phe	Leu	His	Pro	Leu	Leu	Ser	Ser	Lys	Glu	Arg	Glu	Ile	Asp	Asp
				95					100					105
Tyr	Ile	Val	Gln	Ala	Lys	Glu	Arg	Gly	Tyr	Glu	Thr	Met	Val	Asn
				110					115					120
Phe	Gly	Arg	Gln	Gly	Leu	Asn	Leu	Ala	Ala	Thr	Ala	Ala	Val	Thr
				125					130					135
Ala	Ala	Val	Lys	Ser	Gln	Gly	Ala	Ile	Thr	Glu	Arg	Leu	Arg	Ser
				140					145					150
Phe	Ser	Met	His	Asp	Leu	Thr	Thr	Ile	Gln	Gly	Asp	Glu	Pro	Val
				155					160					165
Gly	Gln	Arg	Pro	Tyr	Gln	Pro	Leu	Pro	Glu	Ala	Lys	Lys	Lys	Ser
				170					175					180
Lys	Pro	Ala	Pro	Ser	Glu	Ser	Ala	Gly	Tyr	Gly	Ile	Pro	Leu	Lys
				185					190					195
Asp	Gly	Asp	Glu	Lys	Thr	Asp	Glu	Glu	Ala	Glu	Gly	Pro	Tyr	Ser
				200					205					210
Asp	Asn	Glu	Met	Leu	Thr	His	Lys	Gly	Leu	Arg	Arg	Ser	Gln	Ser
				215					220					225
Met	Lys	Ser	Val	Lys	Thr	Thr	Lys	Gly	Arg	Lys	Glu	Val	Arg	Tyr
				230					235					240
Gly	Ser	Leu	Lys	Tyr	Lys	Val	Lys	Lys	Arg	Pro	Gln	Val	Tyr	Phe
				245					250					255

<210> 11
 <211> 533
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2686765CD1

<400> 11
 Met Ser Gly Thr Leu Glu Ser Leu Ala Asp Asp Val Ser Ser Met

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1	5	10	15
Gly Ser Asp Ser Glu	Ile Asn Gly Leu	Ala Leu Arg Lys Thr	Asp
20	25	30	
Lys Tyr Gly Phe Leu	Gly Gly Ser Gln	Tyr Ser Gly Ser Leu	Glu
35	40	45	
Ser Ser Ile Pro Val	Asp Val Ala Arg	Gln Arg Glu Leu Lys	Trp
50	55	60	
Leu Asp Met Phe Ser	Asn Trp Asp Lys	Trp Leu Ser Arg Arg	Phe
65	70	75	
Gln Lys Val Lys Leu	Arg Cys Arg Lys	Gly Ile Pro Ser Ser	Leu
80	85	90	
Arg Ala Lys Ala Trp	Gln Tyr Leu Ser	Asn Ser Lys Glu Leu	Leu
95	100	105	
Glu Gln Asn Pro Gly	Lys Phe Glu Glu	Leu Arg Ala Pro	Gly
110	115	120	
Asp Pro Lys Trp Leu	Asp Val Ile Glu	Lys Asp Leu His Arg	Gln
125	130	135	
Phe Pro Phe His Glu	Met Phe Ala Ala	Arg Gly Gly His Gly	Gln
140	145	150	
Gln Asp Leu Tyr Arg	Ile Leu Lys Ala	Tyr Thr Ile Tyr Arg	Pro
155	160	165	
Asp Glu Gly Tyr Cys	Gln Ala Gln Ala	Pro Val Ala Ala Val	Leu
170	175	180	
Leu Met His Met Pro	Ala Glu Lys Pro	Phe Gly Ala Trp Val	Gln
185	190	195	
Ile Cys Asp Lys Tyr	Leu Pro Gly Tyr	Tyr Ser Ala Gly Leu	Glu
200	205	210	
Ala Ile Gln Leu Asp	Gly Glu Ile Phe	Phe Ala Leu Leu Arg	Arg
215	220	225	
Ala Ser Pro Leu Ala	His Arg His Leu	Gln Arg Ile Asp	
230	235	240	
Pro Val Leu Tyr Met	Thr Glu Trp Phe	Met Cys Ile Phe Ala	Arg
245	250	255	
Thr Leu Pro Trp Ala	Ser Val Leu Arg	Val Trp Asp Met Phe	Phe
260	265	270	
Cys Glu Gly Val Lys	Ile Ile Phe Arg	Val Ala Leu Val Leu	Leu
275	280	285	
Arg His Thr Leu Gly	Ser Val Glu Lys	Leu Arg Ser Cys Gln	Gly
290	295	300	
Met Tyr Glu Thr Met	Glu Gln Leu Arg	Asn Leu Pro Gln Gln	Cys
305	310	315	
Met Gln Glu Asp Phe	Leu Val His Glu	Val Thr Asn Leu Pro	Val
320	325	330	
Thr Glu Ala Leu Ile	Glu Arg Glu Asn	Ala Ala Gln Leu Lys	Lys
335	340	345	
Trp Arg Glu Thr Arg	Gly Glu Leu Gln	Tyr Arg Pro Ser Arg	Arg
350	355	360	
Leu His Gly Ser Arg	Ala Ile His Glu	Glu Arg Arg Arg Gln	Gln
365	370	375	
Pro Pro Leu Gly Pro	Ser Ser Ser Leu	Ser Leu Pro Gly Leu	
380	385	390	
Lys Ser Arg Gly Ser	Arg Ala Ala Gly	Gly Ala Pro Ser Pro	Pro
395	400	405	
Pro Pro Val Arg Arg	Ala Ser Ala Gly	Pro Ala Pro Gly Pro	Val
410	415	420	
Val Thr Ala Glu Gly	Leu His Pro Ser	Leu Pro Ser Pro Thr	Gly
425	430	435	
Asn Ser Thr Pro Leu	Gly Ser Ser Lys	Glu Thr Arg Lys Gln	Glu
440	445	450	
Lys Glu Arg Gln Lys	Gln Glu Lys Glu	Gln Lys Gln Glu Lys	
455	460	465	
Glu Arg Glu Lys Glu	Arg Gln Lys Gln	Lys Glu Arg Glu Lys	
470	475	480	

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Gln Glu Lys Glu Arg Glu Lys Gln Glu Lys Glu Arg Gln Lys Gln
 485 495
 Glu Lys Lys Ala Gln Gly Arg Lys Leu Ser Leu Arg Arg Lys Ala
 500 505 510
 Asp Gly Pro Pro Gly Pro His Asp Gly Gly Asp Arg Pro Ser Ala
 515 520 525
 Glu Ala Arg Gln Asp Ala Tyr Phe
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<210> 12
 <211> 160
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 3215187CD1

<400> 12
 Met Ala Phe Thr Phe Ala Ala Phe Cys Tyr Met Leu Ser Leu Val
 1 5 10 15
 Leu Cys Ala Ala Leu Ile Phe Phe Ala Ile Trp His Ile Ile Ala
 20 25 30
 Phe Asp Glu Leu Arg Thr Asp Phe Lys Ser Pro Ile Asp Gln Cys
 35 40 45
 Asn Pro Val His Ala Arg Glu Arg Leu Arg Asn Ile Glu Arg Ile
 50 55 60
 Cys Phe Leu Leu Arg Lys Leu Val Leu Pro Glu Tyr Ser Ile His
 65 70 75
 Ser Leu Phe Cys Ile Met Phe Leu Cys Ala Gln Glu Trp Leu Thr
 80 85 90
 Leu Gly Leu Asn Val Pro Leu Leu Phe Tyr His Phe Trp Arg Tyr
 95 100 105
 Phe His Cys Pro Ala Asp Ser Ser Glu Leu Ala Tyr Asp Pro Pro
 110 115 120
 Val Val Met Asn Ala Asp Thr Leu Ser Tyr Cys Gln Lys Glu Ala
 125 130 135
 Trp Cys Lys Leu Ala Phe Tyr Leu Leu Ser Phe Phe Tyr Tyr Leu
 140 145 150
 Tyr Cys Met Ile Tyr Thr Leu Val Ser Ser
 155 160

<210> 13
 <211> 531
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 3500375CD1

<400> 13
 Met Ala Asp Val Leu Ser Val Leu Arg Gln Tyr Asn Ile Gln Lys
 1 5 10 15
 Lys Glu Ile Val Val Lys Gly Asp Glu Val Ile Phe Gly Glu Phe
 20 25 30
 Ser Trp Pro Lys Asn Val Lys Thr Asn Tyr Val Val Trp Gly Thr
 35 40 45
 Gly Lys Glu Gly Gln Pro Arg Glu Tyr Tyr Thr Leu Asp Ser Ile
 50 55 60
 Leu Phe Leu Leu Asn Asn Val His Leu Ser His Pro Val Tyr Val
 65 70 75
 Arg Arg Ala Ala Thr Glu Asn Ile Pro Val Val Arg Arg Pro Asp
 80 85 90
 Arg Lys Asp Leu Leu Gly Tyr Leu Asn Gly Glu Ala Ser Thr Ser

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Ala Ser Ile Asp	95	Ser Ala Pro Leu	100	Ile Gly Leu Gln	105
	110		115		120
Ser Thr Gln Val	Lys	Arg Ala Ala Asp	Glu	Val Leu Ala Glu	Ala
	125		130		135
Lys Lys Pro Arg	Ile	Glu Asp Glu Glu	Cys	Val Arg Leu Asp	Lys
	140		145		150
Glu Arg Leu Ala	Ala	Arg Leu Glu Gly	His	Lys Glu Gly Ile	Val
	155		160		165
Gln Thr Glu Gln	Ile	Arg Ser Leu Ser	Glu	Ala Met Ser Val	Glu
	170		175		180
Lys Ile Ala Ala	Ile	Lys Ala Lys Ile	Met	Ala Lys Lys Arg	Ser
	185		190		195
Thr Ile Lys Thr	Asp	Leu Asp Asp Asp	Ile	Thr Ala Leu Lys	Gln
	200		205		210
Arg Ser Phe Val	Asp	Ala Glu Val Asp	Val	Thr Arg Asp Ile	Val
	215		220		225
Ser Arg Glu Arg	Val	Trp Arg Thr Arg	Thr	Thr Ile Leu Gln	Ser
	230		235		240
Thr Gly Lys Asn	Phe	Ser Lys Asn Ile	Phe	Ala Ile Leu Gln	Ser
	245		250		255
Val Lys Ala Arg	Glu	Glu Gly Arg Ala	Pro	Glu Gln Arg Pro	Ala
	260		265		270
Pro Asn Ala Ala	Pro	Val Asp Pro Thr	Leu	Arg Thr Lys Gln	Pro
	275		280		285
Ile Pro Ala Ala	Tyr	Asn Arg Tyr Asp	Glu	Arg Phe Lys Gly	
	290		295		300
Lys Glu Glu Thr	Glu	Gly Phe Lys Ile	Asp	Thr Met Gly Thr	Tyr
	305		310		315
His Gly Met Thr	Leu	Lys Ser Val Thr	Glu	Gly Ala Ser Ala	Arg
	320		325		330
Lys Thr Gln Thr	Pro	Ala Ala Gln Pro	Val	Pro Arg Pro Val	Ser
	335		340		345
Gln Ala Arg Pro	Pro	Pro Asn Gln Lys	Lys	Gly Ser Arg Thr	Pro
	350		355		360
Ile Ile Ile Ile	Pro	Ala Ala Thr Thr	Ser	Leu Ile Thr Met	Leu
	365		370		375
Asn Ala Lys Asp	Leu	Leu Gln Asp Leu	Lys	Phe Val Pro Ser	Asp
	380		385		390
Glu Lys Lys Lys	Gln	Gly Cys Gln Arg	Glu	Asn Glu Thr Leu	Ile
	395		400		405
Gln Arg Arg Lys	Asp	Gln Met Gln Pro	Gly	Gly Thr Ala Ile	Ser
	410		415		420
Val Thr Val Pro	Tyr	Arg Val Val Asp	Gln	Pro Leu Lys Leu	Met
	425		430		435
Pro Gln Asp Trp	Asp	Arg Val Val Ala	Val	Phe Val Gln Gly	Pro
	440		445		450
Ala Trp Gln Phe	Lys	Gly Trp Pro Trp	Leu	Pro Asp Gly Ser	
	455		460		465
Pro Val Asp Ile	Phe	Ala Lys Ile Lys	Ala	Phe His Leu Lys	Tyr
	470		475		480
Asp Glu Val Arg	Leu	Asp Pro Asn Val	Gln	Lys Trp Asp Val	Thr
	485		490		495
Val Leu Glu Leu	Ser	Tyr His Lys Arg	His	Leu Asp Arg Pro	Val
	500		505		510
Phe Leu Arg Phe	Trp	Glu Thr Leu Asp	Arg	Tyr Met Val Lys	His
	515		520		525
Lys Ser His Leu	Arg	Phe			
	530				

<210> 14

<211> 165

<212> PRT

<213> Homo sapiens

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<220>

<221> misc_feature

<223> Incyte ID No: 5080410CD1

<400> 14

Met	Ala	Ser	Met	Arg	Glu	Ser	Asp	Thr	Gly	Leu	Trp	Leu	His	Asn	
1				5					10					15	
Lys	Leu	Gly	Ala	Thr	Asp	Glu	Leu	Trp	Ala	Pro	Pro	Ser	Ile	Ala	
				20					25					30	
Ser	Leu	Leu	Thr	Ala	Ala	Val	Ile	Asp	Asn	Ile	Arg	Leu	Cys	Phe	
				35					40					45	
His	Gly	Leu	Ser	Ser	Ala	Val	Lys	Leu	Lys	Leu	Leu	Leu	Gly	Thr	
				50					55					60	
Leu	His	Leu	Pro	Arg	Arg	Thr	Val	Asp	Glu	His	Pro	Ile	Leu	Pro	
				65					70					75	
Met	Lys	Gly	Ala	Leu	Met	Glu	Ile	Ile	Gln	Leu	Ala	Ser	Leu	Asp	
				80					85					90	
Ser	Asp	Pro	Trp	Val	Leu	Met	Val	Ala	Asp	Ile	Leu	Lys	Ser	Phe	
				95					100					105	
Pro	Asp	Thr	Gly	Ser	Leu	Asn	Leu	Glu	Leu	Glu	Glu	Gln	Asn	Pro	
				110					115					120	
Asn	Val	Gln	Asp	Ile	Leu	Gly	Glu	Leu	Arg	Glu	Lys	Val	Gly	Glu	
				125					130					135	
Cys	Glu	Ala	Ser	Ala	Met	Leu	Pro	Leu	Glu	Cys	Gln	Tyr	Leu	Asn	
				140					145					150	
Lys	Asn	Ala	Ala	Asp	Asp	Pro	Arg	Gly	Thr	Pro	His	Ser	Pro	Gly	
				155					160					165	

<210> 15

<211> 199

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5218248CD1

<400> 15

Met	Ser	Asn	Met	Glu	Lys	His	Leu	Phe	Asn	Leu	Lys	Phe	Ala	Ala	
1				5					10					15	
Lys	Glu	Leu	Ser	Arg	Ser	Ala	Lys	Lys	Cys	Asp	Lys	Glu	Glu	Lys	
				20					25					30	
Ala	Glu	Lys	Ala	Lys	Ile	Lys	Lys	Ala	Ile	Gln	Lys	Gly	Asn	Met	
				35					40					45	
Glu	Val	Ala	Arg	Ile	His	Ala	Glu	Asn	Ala	Ile	Arg	Gln	Lys	Asn	
				50					55					60	
Gln	Ala	Val	Asn	Phe	Leu	Arg	Met	Ser	Ala	Arg	Val	Asp	Ala	Val	
				65					70					75	
Ala	Ala	Arg	Val	Gln	Thr	Ala	Val	Thr	Met	Gly	Lys	Val	Thr	Lys	
				80					85					90	
Ser	Met	Ala	Gly	Val	Val	Lys	Ser	Met	Asp	Ala	Thr	Leu	Lys	Thr	
				95					100					105	
Met	Asn	Leu	Glu	Lys	Ile	Ser	Ala	Leu	Met	Asp	Lys	Phe	Glu	His	
				110					115					120	
Gln	Phe	Glu	Thr	Leu	Asp	Val	Gln	Thr	Gln	Gln	Met	Glu	Asp	Thr	
				125					130					135	
Met	Ser	Ser	Thr	Thr	Thr	Leu	Thr	Thr	Pro	Gln	Asn	Gln	Val	Asp	
				140					145					150	
Met	Leu	Leu	Gln	Glu	Met	Ala	Asp	Glu	Ala	Gly	Leu	Asp	Leu	Asn	
				155					160					165	
Met	Glu	Leu	Pro	Gln	Gly	Gln	Thr	Gly	Ser	Val	Gly	Thr	Ser	Val	
				170					175					180	
Ala	Ser	Ala	Glu	Gln	Asp	Glu	Leu	Ser	Gln	Arg	Leu	Ala	Arg	Leu	

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Arg Asp Gln Val 185 190 195

<210> 16
 <211> 168
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 058336CD1

<400> 16
 Met Ala Phe Asn Asp Cys Phe Ser Leu Asn Tyr Pro Gly Asn Pro
 1 5 10 15
 Cys Pro Gly Asp Leu Ile Glu Val Phe Arg Pro Gly Tyr Gln His
 20 25 30
 Trp Ala Leu Tyr Leu Gly Asp Gly Tyr Val Ile Asn Ile Ala Pro
 35 40 45
 Val Asp Gly Ile Pro Ala Ser Phe Thr Ser Ala Lys Ser Val Phe
 50 55 60
 Ser Ser Lys Ala Leu Val Lys Met Gln Leu Lys Asp Val Val
 65 70 75
 Gly Asn Asp Thr Tyr Arg Ile Asn Asn Lys Tyr Asp Glu Thr Tyr
 80 85 90
 Pro Pro Leu Pro Val Glu Glu Ile Ile Lys Arg Ser Glu Phe Val
 95 100 105
 Ile Gly Gln Glu Val Ala Tyr Asn Leu Leu Val Asn Asn Cys Glu
 110 115 120
 His Phe Val Thr Leu Arg Tyr Gly Glu Gly Val Ser Glu Gln
 125 130 135
 Ala Asn Arg Ala Ile Ser Thr Val Glu Phe Val Thr Ala Ala Val
 140 145 150
 Gly Val Phe Ser Phe Leu Gly Leu Phe Pro Lys Gly Gln Arg Ala
 155 160 165
 Lys Tyr Tyr

<210> 17
 <211> 162
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 1511488CD1

<400> 17
 Met Leu Arg Ala Val Gly Ser Leu Leu Arg Leu Gly Arg Gly Leu
 1 5 10 15
 Thr Val Arg Cys Gly Pro Gly Ala Pro Leu Glu Ala Thr Arg Arg
 20 25 30
 Pro Ala Pro Ala Leu Pro Pro Arg Gly Leu Pro Cys Tyr Ser Ser
 35 40 45
 Gly Gly Ala Pro Ser Asn Ser Gly Pro Gln Gly His Gly Glu Ile
 50 55 60
 His Arg Val Pro Thr Gln Arg Arg Pro Ser Gln Phe Asp Lys Lys
 65 70 75
 Ile Leu Leu Trp Thr Gly Arg Phe Lys Ser Met Glu Glu Ile Pro
 80 85 90
 Pro Arg Ile Pro Pro Glu Met Ile Asp Thr Ala Arg Asn Lys Ala
 95 100 105
 Arg Val Lys Ala Cys Tyr Ile Met Ile Gly Leu Thr Ile Ile Ala
 110 115 120

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Cys Phe Ala Val Ile Val Ser Ala Lys Arg Ala Val Glu Arg His
 125 135
 Glu Ser Leu Thr Ser Trp Asn Leu Ala Lys Lys Ala Lys Trp Arg
 140 145 150
 Glu Glu Ala Ala Leu Ala Ala Gln Ala Lys Ala Lys
 155 160

<210> 18

<211> 246

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1638819CD1

<400> 18

Met Ala Gly Tyr Leu Lys Leu Val Cys Val Ser Phe Gln Arg Gln
 1 5 10 15
 Gly Phe His Thr Val Gly Ser Arg Cys Lys Asn Arg Thr Gly Ala
 20 25 30
 Glu His Leu Trp Leu Thr Arg His Leu Arg Asp Pro Phe Val Lys
 35 40 45
 Ala Ala Lys Val Glu Ser Tyr Arg Cys Arg Ser Ala Phe Lys Leu
 50 55 60
 Leu Glu Val Asn Glu Arg His Gln Ile Leu Arg Pro Gly Leu Arg
 65 70 75
 Val Leu Asp Cys Gly Ala Ala Pro Gly Ala Trp Ser Gln Val Ala
 80 85 90
 Val Gln Lys Val Asn Ala Ala Gly Thr Asp Pro Ser Ser Pro Val
 95 100 105
 Gly Phe Val Leu Gly Val Asp Leu Leu His Ile Phe Pro Leu Glu
 110 115 120
 Gly Ala Thr Phe Leu Cys Pro Ala Asp Val Thr Asp Pro Arg Thr
 125 130 135
 Ser Gln Arg Ile Leu Glu Val Leu Pro Gly Arg Arg Ala Asp Val
 140 145 150
 Ile Leu Ser Asp Met Ala Pro Asn Ala Thr Gly Phe Arg Asp Leu
 155 160 165
 Asp His Asp Arg Leu Ile Ser Leu Cys Leu Thr Leu Leu Ser Val
 170 175 180
 Thr Pro Asp Ile Leu Gln Pro Gly Gly Thr Phe Leu Cys Lys Thr
 185 190 195
 Trp Ala Gly Ser Gln Ser Arg Arg Leu Gln Arg Arg Leu Thr Glu
 200 205 210
 Glu Phe Gln Asn Val Arg Ile Ile Lys Pro Glu Ala Ser Arg Lys
 215 220 225
 Glu Ser Ser Glu Val Tyr Phe Leu Ala Thr Gln Tyr His Gly Arg
 230 235 240
 Lys Gly Thr Val Lys Gln
 245

<210> 19

<211> 483

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1655123CD1

<400> 19

Met Glu Glu Gly Gly Gly Gly Val Arg Ser Leu Val Pro Gly Gly
 1 5 10 15
 Pro Val Leu Leu Val Leu Cys Gly Leu Leu Glu Ala Ser Gly Gly

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	20		25		30
Gly Arg Ala Leu	Pro Gln Leu Ser Asp	Ile Pro Phe Arg Val			
	35		40		45
Asn Trp Pro Gly Thr	Glu Phe Ser Leu Pro Thr Thr Gly Val Leu				
	50		55		60
Tyr Lys Glu Asp Asn Tyr Val Ile Met Thr Thr Ala His Lys Glu					
	65		70		75
Lys Tyr Lys Cys Ile Leu Pro Leu Val Thr Ser Gly Asp Glu Glu					
	80		85		90
Glu Glu Lys Asp Tyr Lys Gly Pro Asn Pro Arg Glu Leu Leu Glu					
	95		100		105
Pro Leu Phe Lys Gln Ser Ser Cys Ser Tyr Arg Ile Glu Ser Tyr					
	110		115		120
Trp Thr Tyr Glu Val Cys His Gly Lys His Ile Arg Gln Tyr His					
	125		130		135
Glu Glu Lys Glu Thr Gly Gln Lys Ile Asn Ile His Glu Tyr Tyr					
	140		145		150
Leu Gly Asn Met Leu Ala Lys Asn Leu Leu Phe Glu Lys Glu Arg					
	155		160		165
Glu Ala Glu Glu Lys Glu Lys Ser Asn Glu Ile Pro Thr Lys Asn					
	170		175		180
Ile Glu Gly Gln Met Thr Pro Tyr Tyr Pro Val Gly Met Gly Asn					
	185		190		195
Gly Thr Pro Cys Ser Leu Lys Gln Asn Arg Pro Arg Ser Ser Thr					
	200		205		210
Val Met Tyr Ile Cys His Pro Glu Ser Lys His Glu Ile Leu Ser					
	215		220		225
Val Ala Glu Val Thr Thr Cys Glu Tyr Glu Val Val Ile Leu Thr					
	230		235		240
Pro Leu Leu Cys Ser His Pro Lys Tyr Arg Phe Arg Ala Ser Pro					
	245		250		255
Val Asn Asp Ile Phe Cys Gln Ser Leu Pro Gly Ser Pro Phe Lys					
	260		265		270
Pro Leu Thr Leu Arg Gln Leu Glu Gln Gln Glu Glu Ile Leu Arg					
	275		280		285
Val Pro Phe Arg Arg Asn Lys Glu Glu Asp Leu Gln Ser Thr Lys					
	290		295		300
Glu Glu Arg Phe Pro Ala Ile His Lys Ser Ile Ala Ile Gly Ser					
	305		310		315
Gln Pro Val Leu Thr Val Gly Thr Thr His Ile Ser Lys Leu Thr					
	320		325		330
Asp Asp Gln Leu Ile Lys Glu Phe Leu Ser Gly Ser Tyr Cys Phe					
	335		340		345
Arg Gly Gly Val Gly Trp Trp Lys Tyr Glu Phe Cys Tyr Gly Lys					
	350		355		360
His Val His Gln Tyr His Glu Asp Lys Asp Ser Gly Lys Thr Ser					
	365		370		375
Val Val Val Gly Thr Trp Asn Gln Glu Glu His Ile Glu Trp Ala					
	380		385		390
Lys Lys Asn Thr Ala Arg Ala Tyr His Leu Gln Asp Asp Gly Thr					
	395		400		405
Gln Thr Val Arg Met Val Ser His Phe Tyr Gly Asn Gly Asp Ile					
	410		415		420
Cys Asp Ile Thr Asp Lys Pro Arg Gln Val Thr Val Lys Leu Lys					
	425		430		435
Cys Lys Glu Ser Asp Ser Pro His Ala Val Thr Val Tyr Met Leu					
	440		445		450
Glu Pro His Ser Cys Gln Tyr Ile Leu Gly Val Glu Ser Pro Val					
	455		460		465
Ile Cys Lys Ile Leu Asp Thr Ala Asp Asn Gly Leu Leu Ser					
	470		475		480
Leu Pro Asn					

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<210> 20
 <211> 280
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2553926CD1

<400> 20
 Met Glu Ala Ala Glu Thr Glu Ala Glu Ala Ala Leu Glu Val
 1 5 10 15
 Leu Ala Glu Val Ala Gly Ile Leu Glu Pro Val Gly Leu Gln Glu
 20 25 30
 Glu Ala Glu Leu Pro Ala Lys Ile Leu Val Glu Phe Val Val Asp
 35 40 45
 Ser Gln Lys Lys Asp Lys Leu Leu Cys Ser Gln Leu Gln Val Ala
 50 55 60
 Asp Phe Leu Gln Asn Ile Leu Ala Gln Glu Asp Thr Ala Lys Gly
 65 70 75
 Leu Asp Pro Leu Ala Ser Glu Asp Thr Ser Arg Gln Lys Ala Ile
 80 85 90
 Ala Ala Lys Glu Gln Trp Lys Glu Leu Lys Ala Thr Tyr Arg Glu
 95 100 105
 His Val Glu Ala Ile Lys Ile Gly Leu Thr Lys Ala Leu Thr Gln
 110 115 120
 Met Glu Glu Ala Gln Arg Lys Arg Thr Gln Leu Arg Glu Ala Phe
 125 130 135
 Glu Gln Leu Gln Ala Lys Lys Gln Met Ala Met Glu Lys Arg Arg
 140 145 150
 Ala Val Gln Asn Gln Trp Gln Leu Gln Gln Glu Lys His Leu Gln
 155 160 165
 His Leu Ala Glu Val Ser Ala Glu Val Arg Glu Arg Lys Thr Gly
 170 175 180
 Thr Gln Gln Glu Leu Asp Gly Val Phe Gln Lys Leu Gly Asn Leu
 185 190 195
 Lys Gln Gln Ala Glu Gln Glu Arg Asp Lys Leu Gln Arg Tyr Gln
 200 205 210
 Thr Phe Leu Gln Leu Leu Tyr Thr Leu Gln Gly Lys Leu Leu Phe
 215 220 225
 Pro Glu Ala Glu Ala Glu Ala Glu Asn Leu Pro Asp Asp Lys Pro
 230 235 240
 Gln Gln Pro Thr Arg Pro Gln Glu Gln Ser Thr Gly Asp Thr Met
 245 250 255
 Gly Arg Asp Pro Gly Val Ser Phe Lys Phe Ser Lys Ala Val Gly
 260 265 270
 Leu Gln Pro Ala Gly Asp Val Asn Leu Pro
 275 280

<210> 21
 <211> 425
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2800717CD1

<400> 21
 Met Gly Glu Asp Ala Ala Gln Ala Glu Lys Phe Gln His Pro Gly
 1 5 10 15
 Ser Asp Met Arg Gln Glu Lys Pro Ser Ser Pro Ser Pro Met Pro
 20 25 30
 Ser Ser Thr Pro Ser Pro Ser Leu Asn Leu Gly Asn Thr Glu Glu

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Ala Ile Arg Asp	35	Asn Ser Gln Val Asn Ala	40	Val Thr Val Leu Thr	45
Leu Leu Asp Lys	50	Leu Val Asn Met Leu Asp	55	Ala Val Gln Glu Asn	60
Gln His Lys Met	65	Gln Arg Gln Ile Ser	70	Leu Glu Gly Ser Val	75
Lys Gly Ile Gln	80	Asn Asp Leu Thr Lys	85	Leu Ser Lys Tyr Gln Ala	90
Ser Thr Ser Asn Thr	95	Val Ser Lys Leu Leu	100	Glu Lys Ser Arg Lys	105
Val Ser Ala His Thr	110	Arg Ala Val Lys Glu	115	Arg Met Asp Arg Gln	120
Cys Ala Gln Val Lys	125	Arg Leu Glu Asn Asn	130	His Ala Gln Leu Leu	135
Arg Arg Asn His Phe	140	Lys Val Leu Ile Phe	145	Gln Glu Glu Asn Glu	150
Ile Pro Ala Ser Val	155	Phe Val Lys Gln Pro	160	Val Ser Gly Ala Val	165
Glu Gly Lys Glu Glu	170	Leu Pro Asp Glu Asn	175	Lys Ser Leu Glu Glu	180
Thr Leu His Thr Val	185	Asp Leu Ser Ser Asp	190	Asp Asp Leu Pro His	195
Asp Glu Glu Ala Leu	200	Glu Asp Ser Ala Glu	205	Lys Val Glu Glu Glu	210
Ser Arg Ala Glu Lys	215	Ile Lys Arg Ser Ser	220	Leu Lys Lys Val Asp	225
Ser Leu Lys Lys Ala	230	Phe Ser Arg Gln Asn	235	Ile Glu Lys Lys Met	240
Asn Lys Leu Gly Thr	245	Lys Ile Val Ser Val	250	Glu Arg Arg Glu Lys	255
Ile Lys Lys Ser Leu	260	Thr Ser Asn His Gln	265	Lys Ile Ser Ser Gly	270
Lys Ser Ser Pro Phe	275	Lys Val Ser Pro Leu	280	Thr Phe Gly Arg Lys	285
Lys Val Arg Glu Gly	290	Glu Ser His Ala Glu	295	Asn Glu Thr Lys Ser	300
Glu Asp Leu Pro Ser	305	Ser Ser Glu Gln Met	310	Pro Asn Asp Gln Glu	315
Glu Ser Phe Ala Glu	320	Gly His Ser Glu Ala	325	Ser Leu Ala Ser Ala	330
Leu Val Glu Gly Glu	335	Ile Ala Glu Glu Ala	340	Glu Lys Ala Thr	345
Ser Arg Gly Ser Asn	350	Ser Gly Met Asp Ser	355	Asn Ile Asp Leu Thr	360
Ile Val Glu Asp Glu	365	Glu Glu Glu Ser Val	370	Ala Leu Glu Gln Ala	375
Gln Lys Val Arg Tyr	380	Glu Gly Ser Tyr Glu	385	Thr Ser Glu Glu Glu	390
Ala Glu Arg Ser Asp	395	Gly Asp Pro Val Gln	400	Pro Ala Val Leu Gln	405
Val His Gln Thr Ser	410		415		420
	425				

<210> 22

<211> 128

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5664154CD1

<400> 22

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Met Glu Ser Lys Glu Glu Arg Ala Leu Asn Asn Leu Ile Val Glu
 1      5      10
Asn Val Asn Gln Glu Asn Asp Glu Lys Asp Glu Lys Glu Gln Val
 20      25      30
Ala Asn Lys Gly Glu Pro Leu Ala Leu Pro Leu Asn Val Ser Glu
 35      40      45
Tyr Cys Val Pro Arg Gly Asn Arg Arg Phe Arg Val Arg Gln
 50      55      60
Pro Ile Leu Gln Tyr Arg Trp Asp Ile Met His Arg Leu Gly Glu
 65      70      75
Pro Gln Ala Arg Met Arg Glu Glu Asn Met Glu Arg Ile Gly Glu
 80      85      90
Glu Val Arg Gln Leu Met Glu Lys Leu Arg Glu Lys Gln Leu Ser
 95      100      105
His Ser Leu Arg Ala Val Ser Thr Asp Pro Pro His His Asp His
 110      115      120
His Asp Glu Phe Cys Leu Met Pro
 125

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<210> 23

<211> 113

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 017900CD1

<400> 23

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Met Asp Gly Arg Val Gln Leu Ile Lys Ala Leu Leu Ala Leu Pro
 1      5      10      15
Ile Arg Pro Ala Thr Arg Arg Trp Arg Asn Pro Ile Pro Phe Pro
 20      25      30
Glu Thr Phe Asp Gly Asp Thr Asp Arg Leu Pro Glu Phe Ile Val
 35      40      45
Gln Thr Gly Ser Tyr Met Phe Val Asp Glu Asn Thr Phe Ser Ser
 50      55      60
Asp Ala Leu Lys Val Thr Phe Leu Ile Thr Arg Leu Thr Gly Pro
 65      70      75
Ala Leu Gln Trp Val Ile Pro Tyr Ile Lys Lys Glu Ser Pro Leu
 80      85      90
Leu Asn Asp Tyr Arg Gly Phe Leu Ala Glu Met Lys Arg Val Phe
 95      100      105
Gly Trp Glu Glu Asp Glu Asp Phe
 110

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<210> 24

<211> 308

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 035102CD1

<400> 24

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Met Leu Gln Thr Pro Glu Ser Arg Gly Leu Pro Val Pro Gln Ala
 1      5      10      15
Glu Gly Glu Lys Asp Gly Gly His Asp Gly Thr Arg Ala Pro
 20      25      30
Thr Ala Ser Gln Glu Arg Pro Lys Glu Glu Leu Gly Ala Gly Arg
 35      40      45
Glu Glu Gly Ala Ala Glu Pro Ala Leu Thr Arg Lys Gly Ala Arg
 50      55      60
Ala Leu Ala Ala Lys Ser Leu Ala Arg Arg Arg Ala Tyr Arg Arg

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Leu Asn Arg Thr	65	Val Ala Glu Leu Val	70	Phe Leu Leu Val	75
Asp Lys Lys Lys	80	Ser Pro Ile Thr Arg	85	Glu Met Val Lys	90
Val Ile Gly Asp	95	Leu Lys Ile Leu Phe	100	Pro Asp Ile Ile Ala	105
Ala Ala Glu His	110	Leu Arg Tyr Val Phe	115	Gly Phe Glu Leu Lys	120
Phe Asp Arg Lys	125	His His Thr Tyr Ile	130	Leu Ile Asn Lys Leu	135
Pro Leu Glu Glu	140	Glu Glu Glu Glu Glu	145	Asp Leu Gly Gly Asp	150
Pro Arg Leu Gly	155	Leu Leu Met Met Ile	160	Gly Leu Ile Tyr	165
Arg Gly Asn Ser	170	Ala Arg Glu Ala Gln	175	Val Trp Glu Met Leu	180
Arg Leu Gly Val	185	Gln Pro Ser Lys Tyr	190	His Phe Leu Phe Gly	195
Pro Lys Arg Leu	200	Ile Met Glu Asp Phe	205	Val Gln Gln Arg Tyr	210
Ser Tyr Arg Arg	215	Val Pro His Thr Asn	220	Pro Pro Ala Tyr Glu	225
Ser Trp Gly Pro	230	Arg Ser Asn Leu Glu	235	Ile Ser Lys Met Glu	240
Leu Gly Phe Val	245	Ala Lys Leu His Lys	250	Lys Glu Pro Gln His	255
Pro Val Gln Tyr	260	Arg Glu Ala Leu Ala	265	Asp Glu Ala Asp Arg	270
Arg Ala Lys Ala	275	Arg Ala Glu Ala Ser	280	Met Arg Ala Arg Ala	285
Ala Arg Ala Gly	290	Ile His Leu Trp	295		300

<210> 25

<211> 221

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 259983CD1

<400> 25

Met Phe Gly Phe	1	His Lys Pro Lys Met	10	Tyr Arg Ser Ile Glu	15
Cys Cys Ile Cys	5	Arg Ala Lys Ser Ser	20	Ser Ser Arg Phe Thr	25
Ser Lys Arg Tyr	20	Glu Lys Asp Phe Gln	25	Ser Cys Phe Gly Leu	30
Glu Thr Arg Ser	35	Gly Asp Ile Cys Asn	40	Ala Cys Val Leu Leu	45
Lys Arg Trp Lys	50	Lys Leu Pro Ala Gly	55	Ser Lys Lys Asn Trp	60
His Val Val Asp	65	Ala Arg Ala Gly Pro	70	Ser Leu Lys Thr Thr	75
Lys Pro Lys Lys	80	Val Lys Thr Leu Ser	85	Gly Asn Arg Ile Lys	90
Asn Gln Ile Ser	95	Leu Gln Lys Glu Phe	100	Lys Arg His Asn Ser	105
Asp Ala His Ser	110	Thr Thr Ser Ser Ala	115	Ser Pro Ala Gln Ser	120
Cys Tyr Ser Asn	125	Gln Ser Asp Asp Gly	130	Ser Asp Thr Glu Met	135
	140		145		150

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Ser Gly Ser Asn Arg Thr Pro Val Phe Ser Phe Leu Asp Leu Thr
155 160
Tyr Trp Lys Arg Gln Lys Ile Cys Cys Gly Ile Ile Tyr Lys Gly
170 175
Arg Phe Gly Glu Val Leu Ile Asp Thr His Leu Phe Lys Pro Cys
185 190
Cys Ser Asn Lys Lys Ala Ala Ala Glu Lys Pro Glu Glu Gln Gly
200 210
Pro Glu Pro Leu Pro Ile Ser Thr Gln Glu Trp
215 220

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<210> 26

<211> 402

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 926810CD1

<400> 26

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Met Ala Ser Ile Ile Ala Arg Val Gly Asn Ser Arg Arg Leu Asn
1 5 10 15
Ala Pro Leu Pro Pro Trp Ala His Ser Met Leu Arg Ser Leu Gly
20 25 30
Arg Ser Leu Gly Pro Ile Met Ala Ser Met Ala Asp Arg Asn Met
35 40 45
Lys Leu Phe Ser Gly Arg Val Val Pro Ala Gln Gly Glu Glu Thr
50 55 60
Phe Glu Asn Trp Leu Thr Gln Val Asn Gly Val Leu Pro Asp Trp
65 70 75
Asn Met Ser Glu Glu Glu Lys Leu Lys Arg Leu Met Lys Thr Leu
80 85 90
Arg Gly Pro Ala Arg Glu Val Met Arg Val Leu Gln Ala Thr Asn
95 100 105
Pro Asn Leu Ser Val Ala Asp Phe Leu Arg Ala Met Lys Leu Val
110 115 120
Phe Gly Glu Ser Glu Ser Ser Val Thr Ala His Gly Lys Phe Phe
125 130 135
Asn Thr Leu Gln Ala Gln Gly Glu Lys Ala Ser Leu Tyr Val Ile
140 145 150
Arg Leu Glu Val Gln Leu Gln Asn Ala Ile Gln Ala Gly Ile Ile
155 160 165
Ala Glu Lys Asp Ala Asn Arg Thr Arg Leu Gln Gln Leu Leu Leu
170 175 180
Gly Gly Glu Leu Ser Arg Asp Leu Arg Leu Arg Leu Lys Asp Phe
185 190 195
Leu Arg Met Tyr Ala Asn Glu Gln Glu Arg Leu Pro Asn Phe Leu
200 205 210
Glu Leu Ile Arg Met Val Arg Glu Glu Glu Asp Trp Asp Asp Ala
215 220 225
Phe Ile Lys Arg Lys Arg Pro Lys Arg Ser Glu Ser Met Val Glu
230 235 240
Arg Ala Val Ser Pro Val Ala Phe Gln Gly Ser Pro Pro Ile Val
245 250 255
Ile Gly Ser Ala Asp Cys Asn Val Ile Glu Ile Asp Asp Thr Leu
260 265 270
Asp Asp Ser Asp Glu Asp Val Ile Leu Val Glu Ser Gln Asp Pro
275 280 285
Pro Leu Pro Ser Trp Gly Ala Pro Pro Leu Arg Asp Arg Ala Arg
290 295 300
Pro Gln Asp Glu Val Leu Val Ile Asp Ser Pro His Asn Ser Arg
305 310 315
Ala Gln Phe Pro Ser Thr Ser Gly Gly Ser Gly Tyr Lys Asn Asn

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	320		325		330
Gly Pro Gly Glu	Met Arg Arg Ala Arg	Lys Arg Lys His Thr	Ile		
	335		340		345
Arg Cys Ser Tyr	Cys Gly Glu Glu Gly	His Ser Lys Glu Thr	Cys		
	350		355		360
Asp Asn Glu Ser	Asp Lys Ala Gln Val	Phe Glu Asn Leu Ile	Ile		
	365		370		375
Thr Leu Gln Glu	Leu Thr His Thr Glu	Met Glu Arg Ser Arg	Val		
	380		385		390
Ala Pro Gly Glu	Tyr Asn Asp Phe Ser	Glu Pro Leu			
	395		400		

<210> 27
 <211> 93
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 1398816CD1

<400> 27	
Met Ser Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp	
1 5 10 15	
Gln Gly Ser Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val	
20 25 30	
Pro Val Gly Ile Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu	
35 40 45	
Tyr Lys Leu Lys Ser Arg Gly Asn Thr Lys Met Ser Ile His Leu	
50 55 60	
Ile His Met Arg Val Ala Ala Gln Gly Phe Val Val Gly Ala Met	
65 70 75	
Thr Val Gly Met Gly Tyr Ser Met Tyr Arg Glu Phe Trp Ala Lys	
80 85 90	
Pro Lys Pro	

<210> 28
 <211> 353
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 1496820CD1

<400> 28	
Met Asn Arg Glu Asp Arg Asn Val Leu Arg Met Lys Glu Arg Glu	
1 5 10 15	
Arg Arg Asn Gln Glu Ile Gln Gln Gly Glu Asp Ala Phe Pro Pro	
20 25 30	
Ser Ser Pro Leu Phe Ala Glu Pro Tyr Lys Val Thr Ser Lys Glu	
35 40 45	
Asp Lys Leu Ser Ser Arg Ile Gln Ser Met Leu Gly Asn Tyr Asp	
50 55 60	
Glu Met Lys Asp Phe Ile Gly Asp Arg Ser Ile Pro Lys Leu Val	
65 70 75	
Ala Ile Pro Lys Pro Thr Val Pro Pro Ser Ala Asp Glu Lys Ser	
80 85 90	
Asn Pro Asn Phe Phe Glu Gln Arg His Gly Ser His Gln Ser	
95 100 105	
Ser Lys Trp Thr Pro Val Gly Pro Ala Pro Ser Thr Ser Gln Ser	
110 115 120	
Gln Lys Arg Ser Ser Gly Leu Gln Ser Gly His Ser Ser Gln Arg	
125 130 135	

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Thr Ser Ala Gly Ser Ser Ser Gly Thr Asn Ser Ser Gly Gln Arg
140 150
His Asp Arg Glu Ser Tyr Asn Asn Ser Gly Ser Ser Ser Arg Lys
155 165
Lys Gly Gln His Gly Ser Glu His Ser Lys Ser Arg Ser Ser Ser
170 180
Pro Gly Lys Pro Gln Ala Val Ser Ser Leu Asn Ser Ser His Ser
185 195
Arg Ser His Gly Asn Asp His His Ser Lys Glu His Gln Arg Ser
200 210
Lys Ser Pro Arg Asp Pro Asp Ala Asn Trp Asp Ser Pro Ser Arg
215 225
Val Pro Phe Ser Ser Gly Gln His Ser Thr Gln Ser Phe Pro Pro
230 240
Ser Leu Met Ser Lys Ser Asn Ser Met Leu Gln Lys Pro Thr Ala
245 255
Tyr Val Arg Pro Met Asp Gly Gln Glu Ser Met Glu Pro Lys Leu
260 270
Ser Ser Glu His Tyr Ser Ser Gln Ser His Gly Asn Ser Met Thr
275 285
Glu Leu Lys Pro Ser Ser Lys Ala His Leu Thr Lys Leu Lys Ile
290 300
Pro Ser Gln Pro Leu Asp Ala Ser Ala Ser Gly Asp Val Ser Cys
305 315
Val Asp Glu Ile Leu Lys Glu Met Thr His Ser Trp Pro Pro Pro
320 330
Leu Thr Ala Ile His Thr Pro Cys Lys Thr Glu Pro Ser Lys Phe
335 345
Pro Phe Pro Thr Lys Val Ser Lys
350

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<210> 29

<211> 120

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1514559CD1

<400> 29

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Met Ser Glu Pro Ala Gly Asp Val Arg Gln Asn Pro Cys Gly Ser
1 5 10 15
Lys Ala Cys Arg Arg Leu Phe Gly Pro Val Asp Ser Glu Gln Leu
20 25 30
Ser Arg Asp Cys Asp Ala Leu Met Ala Gly Cys Ile Gln Glu Ala
35 40 45
Arg Glu Arg Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu Glu
50 55 60
Gly Asp Phe Ala Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys
65 70 75
Leu Tyr Leu Pro Thr Trp Ser Ala Gly Trp Tyr Pro Leu Glu Gly
80 85 90
Cys Gly Ser Phe Pro Ser Leu Ser Gln Ala Val Met Lys Phe Thr
95 100 105
Pro Phe Pro Gly His Ser Asp Leu Asn Ser Phe Ser Phe Glu Lys
110 115 120

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<210> 30

<211> 144

<212> PRT

<213> Homo sapiens

<220>

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<221> misc_feature

<223> Incyte ID No: 1620092CD1

<400> 30

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Met Arg Ser Cys Phe Arg Leu Cys Glu Arg Asp Val Ser Ser Ser
 1          5          10          15
Leu Arg Leu Thr Arg Ser Ser Asp Leu Lys Arg Ile Asn Gly Phe
 20          25          30
Cys Thr Lys Pro Gln Glu Ser Pro Gly Ala Pro Ser Arg Thr Tyr
 35          40          45
Asn Arg Val Pro Leu His Lys Pro Thr Asp Trp Gln Lys Lys Ile
 50          55          60
Leu Ile Trp Ser Gly Arg Phe Lys Lys Glu Asp Glu Ile Pro Glu
 65          70          75
Thr Val Ser Leu Glu Met Leu Asp Ala Ala Lys Asn Lys Met Arg
 80          85          90
Val Lys Ile Ser Tyr Leu Met Ile Ala Leu Thr Val Val Gly Cys
 95          100          105
Ile Phe Met Val Ile Glu Gly Lys Lys Ala Ala Gln Arg His Glu
 110          115          120
Thr Leu Thr Ser Leu Asn Leu Glu Lys Lys Ala Arg Leu Lys Glu
 125          130          135
Glu Ala Ala Met Lys Ala Lys Thr Glu
 140

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<210> 31

<211> 933

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1678765CD1

<400> 31

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Met Phe Tyr Leu Glu Asp Asp Lys Glu Asp Glu Val Val Cys Lys
 1          5          10          15
Gly Ser Leu Ser Lys Thr Gln Asp Val Tyr His Asp Lys Ser Pro
 20          25          30
Pro Gly Ile Leu Ser Gln Thr Met Asn Tyr Val Gly Gln Leu Ala
 35          40          45
Gly Gln Val Ile Val Thr Val Lys Glu Leu Tyr Lys Gly Ile Asn
 50          55          60
Gln Ala Thr Leu Ser Gly Cys Ile Asp Val Ile Val Val Gln Gln
 65          70          75
Gln Asp Gly Ser Tyr Gln Cys Ser Pro Phe His Val Arg Phe Gly
 80          85          90
Lys Leu Gly Val Leu Arg Ser Lys Glu Lys Val Ile Asp Ile Glu
 95          100          105
Ile Asn Gly Ser Ala Val Asp Leu His Met Lys Leu Gly Asp Asn
 110          115          120
Gly Glu Ala Phe Phe Val Glu Glu Thr Glu Glu Glu Tyr Glu Lys
 125          130          135
Leu Pro Ala Tyr Leu Ala Thr Ser Pro Ile Pro Thr Glu Asp Gln
 140          145          150
Phe Phe Lys Asp Ile Asp Thr Pro Leu Val Lys Ser Gly Gly Asp
 155          160          165
Glu Thr Pro Ser Gln Ser Ser Asp Ile Ser His Val Leu Glu Thr
 170          175          180
Glu Thr Ile Phe Thr Pro Ser Ser Val Lys Lys Lys Lys Arg Arg
 185          190          195
Arg Lys Lys Tyr Lys Gln Asp Ser Lys Lys Glu Glu Gln Ala Ala
 200          205          210
Ser Ala Ala Ala Glu Asp Thr Cys Asp Val Gly Val Ser Ser Asp

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Asp	Asp	Lys	Gly	215	Gln	Ala	Ala	Arg	220	Gly	Ser	Ser	Asn	Ala	225	Ser
Leu	Lys	Glu	Glu	230	Cys	Lys	Glu	Pro	235	Leu	Phe	His	Ser	Gly	240	Gly
Asp	His	Tyr	Pro	245	Leu	Ser	Asp	Gly	250	Trp	Ser	Pro	Leu	Glu	255	Thr
Thr	Tyr	Pro	Gln	260	Thr	Ala	Cys	Pro	265	Ser	Asp	Ser	Glu	Leu	270	Glu
Val	Lys	Pro	Ala	275	Ser	Leu	Leu	Arg	280	Ser	Glu	Tyr	His	Met	285	Glu
Trp	Thr	Trp	Gly	290	Gly	Phe	Pro	Glu	295	Thr	Lys	Val	Ser	Lys	300	Arg
Glu	Arg	Ser	Asp	305	His	His	Pro	Arg	310	Ala	Thr	Ile	Thr	Pro	315	Ser
Glu	Asn	Thr	His	320	Arg	Val	Ile	Pro	325	Ser	Glu	Asp	Asn	Leu	330	Ile
Ser	Glu	Val	Glu	335	Lys	Asp	Ala	Ser	340	Glu	Asp	Thr	Val	Cys	345	Thr
Ile	Val	Lys	Pro	350	Pro	Arg	Ala	Leu	355	Gly	Thr	Gln	Met	Ser	360	Asp
Pro	Thr	Ser	Val	365	Glu	Leu	Leu	Glu	370	Pro	Pro	Leu	Glu	Ser	375	Thr
Gln	Ile	Ser	Ser	380	Met	Leu	Asp	Ala	385	His	Leu	Pro	Asn	Ala	390	Ala
Leu	Ala	Glu	Ala	395	Pro	Ser	Glu	Ser	400	Pro	Ala	Ala	Lys	Val	405	Asp
Ser	Pro	Ser	Lys	410	Lys	Lys	Gly	Val	415	Lys	Arg	Ile	Gln	His	420	Gln
Gly	Pro	Asp	Asp	425	Ile	Tyr	Leu	Asp	430	Leu	Lys	Gly	Leu	Glu	435	Pro
Glu	Val	Ala	Ala	440	Leu	Tyr	Phe	Pro	445	Ser	Glu	Ser	Glu	Pro	450	Gly
Ser	Arg	Gln	Trp	455	Pro	Glu	Ser	Asp	460	Thr	Ser	Gly	Ser	Gln	465	Ser
Pro	Gln	Ser	Val	470	Gly	Ser	Ala	Ala	475	Asp	Ser	Gly	Thr	Glu	480	Cys
Leu	Ser	Asp	Ser	485	Met	Asp	Leu	Pro	490	Asp	Val	Thr	Leu	Ser	495	Leu
Cys	Gly	Gly	Leu	500	Glu	Asn	Gly	Lys	505	Ile	Ser	Lys	Glu	Lys	510	Phe
Met	Glu	His	Ile	515	Thr	Tyr	His	Glu	520	Phe	Ala	Glu	Asn	Pro	525	Gly
Leu	Ile	Asp	Asn	530	Pro	Asn	Leu	Val	535	Arg	Ile	Tyr	Asn	Arg	540	Tyr
Tyr	Asn	Trp	Ala	545	Leu	Ala	Ala	Pro	550	Ile	Leu	Ser	Leu	Gln	555	Val
Phe	Gln	Lys	Ser	560	Leu	Pro	Lys	Ala	565	Val	Glu	Ser	Trp	Val	570	Lys
Asp	Lys	Met	Pro	575	Lys	Ser	Gly	Arg	580	Trp	Trp	Phe	Trp	Arg	585	Lys
Arg	Glu	Ser	Met	590	Lys	Gln	Leu	Pro	595	Glu	Ser	Lys	Glu	Gly	600	Lys
Ser	Glu	Ala	Pro	605	Pro	Ala	Ser	Asp	610	Pro	Ser	Ser	Ser	Lys	615	Glu
Pro	Ala	Gly	Ala	620	Arg	Pro	Ala	Glu	625	Asp	Ser	Ser	Ser	Asp	630	Glu
Gly	Ser	Gln	Glu	635	Glu	Glu	Ser	Ile	640	Thr	Val	Asp	Pro	Ile	645	Pro
Thr	Glu	Pro	Leu	650	Ser	His	Gly	Ser	655	Thr	Ser	Tyr	Lys	Lys	660	Ser
Leu	Arg	Leu	Ser	665	Asp	Gln	Ile	Ala	670	Lys	Leu	Lys	Leu	His	675	Asp
				680					685						690	

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Gly Pro Asn Asp Val Val Phe Ser Ile Thr Thr Gln Tyr Gln Gly
 695 700
 Thr Cys Arg Cys Ala Gly Thr Ile Tyr Leu Trp Asn Trp Asn Asp
 710 715
 Lys Ile Ile Ile Ser Asp Ile Asp Gly Thr Ile Thr Lys Ser Asp
 725 730
 Ala Leu Gly Gln Ile Leu Pro Gln Leu Gly Lys Asp Trp Thr His
 740 745
 Gln Gly Ile Ala Lys Leu Tyr His Ser Ile Asn Glu Asn Gly Tyr
 755 760
 Lys Phe Leu Tyr Cys Ser Ala Arg Ala Ile Gly Met Ala Asp Met
 770 775
 Thr Arg Gly Tyr Leu His Trp Val Asn Asp Lys Gly Thr Ile Leu
 785 790
 Pro Arg Gly Pro Leu Met Leu Ser Pro Ser Ser Leu Phe Ser Ala
 800 805
 Phe His Arg Glu Val Ile Glu Lys Lys Pro Glu Lys Phe Lys Ile
 815 820
 Glu Cys Leu Asn Asp Ile Lys Asn Leu Phe Ala Pro Ser Lys Gln
 830 835
 Pro Phe Tyr Ala Ala Phe Gly Asn Arg Pro Asn Asp Val Tyr Ala
 845 850
 Tyr Thr Gln Val Gly Val Pro Asp Cys Arg Ile Phe Thr Val Asn
 860 865
 Pro Lys Gly Glu Leu Ile Gln Glu Arg Thr Lys Gly Asn Lys Ser
 875 880
 Ser Tyr His Arg Leu Ser Glu Leu Val Glu His Val Phe Pro Leu
 890 895
 Leu Ser Lys Glu Gln Asn Ser Ala Phe Pro Cys Pro Glu Phe Ser
 905 910
 Ser Phe Cys Tyr Trp Arg Asp Pro Ile Pro Glu Val Asp Leu Asp
 920 925
 Asp Leu Ser 930

<210> 32

<211> 268

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1708229CD1

<400> 32

Met Leu Gly Asp His Cys Ser Leu Pro Glu Asp Gln Ala Arg Pro
 1 5 10 15
 Gly Gln Ser Leu Gln Ser Gly Leu Cys Cys Lys Met Val Leu Gln
 20 25 30
 Ala Val Ser Lys Val Leu Arg Lys Ser Lys Ala Lys Pro Asn Gly
 35 40 45
 Lys Lys Pro Ala Ala Glu Glu Arg Lys Ala Tyr Leu Glu Pro Glu
 50 55 60
 His Thr Lys Ala Arg Ile Thr Asp Phe Gln Phe Lys Glu Leu Val
 65 70 75
 Val Leu Pro Arg Glu Ile Asp Leu Asn Glu Trp Leu Ala Ser Asn
 80 85 90
 Thr Thr Thr Phe Phe His His Ile Asn Leu Gln Tyr Ser Thr Ile
 95 100 105
 Ser Glu Phe Cys Thr Gly Glu Thr Cys Gln Thr Met Ala Val Cys
 110 115 120
 Asn Thr Gln Tyr Tyr Trp Tyr Asp Glu Arg Gly Lys Lys Val Lys
 125 130 135
 Cys Thr Ala Pro Gln Tyr Val Asp Phe Val Met Ser Ser Val Gln

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Lys	Leu	Val	Thr	140	Glu	Asp	Val	Phe	145	Pro	Thr	Lys	Tyr	Gly	150
				155					160						165
Glu	Phe	Pro	Ser	170	Phe	Glu	Ser	Leu	175	Val	Arg	Lys	Ile	Cys	180
				185					190						195
His	Leu	Phe	His	200	Val	Leu	Ala	His	205	Ile	Trp	Ala	His	Phe	210
				215					220						225
Glu	Thr	Leu	Ala	230	Leu	Glu	Leu	His	235	His	Leu	Asn	Thr	Leu	240
				245					250						255
Val	His	Phe	Ile	260	Leu	Phe	Ala	Arg	265	Glu	Asn	Leu	Leu	Asp	270
				275					280						285
Lys	Glu	Thr	Ala	290	Met	Asp	Asp	Leu	295	Thr	Glu	Val	Leu	Cys	300
				305					310						315
Gly	Ala	Gly	Gly	320	Val	His	Ser	Gly	325	Gly	Asp	Gly	Ala	Gly	330
				335					340						345
Ser	Gly	Gly	Pro	350	Ala	Gln	Asn	His	355	Val	Lys	Glu	Arg		360
				365					370						375

<210> 33'

<211> 337

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1806454CD1

<400> 33

Met	Leu	Leu	Gly	1	Leu	Ala	Ala	Met	10	Glu	Leu	Lys	Val	Trp	15
				5					20						25
Gly	Ile	Gln	Arg	20	Val	Val	Cys	Gly	25	Val	Ser	Glu	Gln	Thr	30
				35					40						45
Gln	Glu	Val	Val	35	Ile	Ala	Leu	Ala	40	Gln	Ala	Ile	Gly	Gln	50
				50					55						60
Arg	Phe	Val	Leu	50	Val	Gln	Arg	Leu	55	Arg	Glu	Lys	Glu	Arg	65
				65					70						75
Leu	Pro	Gln	Glu	65	Cys	Pro	Val	Gly	70	Ala	Gln	Ala	Thr	Cys	80
				80					85						90
Phe	Ala	Ser	Asp	80	Val	Gln	Phe	Val	85	Leu	Arg	Arg	Thr	Gly	95
				95					100						105
Leu	Ala	Gly	Arg	95	Pro	Ser	Ser	Asp	100	Ser	Cys	Pro	Pro	Pro	110
				110					115						115
Cys	Leu	Ile	Arg	110	Ala	Ser	Leu	Pro	115	Val	Lys	Pro	Arg	Ala	120
				125					130						135
Gly	Cys	Glu	Pro	125	Arg	Lys	Thr	Leu	130	Thr	Pro	Glu	Pro	Ala	140
				140					145						150
Leu	Ser	Arg	Pro	140	Gly	Pro	Ala	Ala	145	Pro	Val	Thr	Pro	Thr	155
				155					160						165
Cys	Cys	Thr	Asp	155	Leu	Arg	Gly	Leu	160	Glu	Arg	Val	Gln	Arg	170
				170					175						180
Ala	Glu	Glu	Leu	170	His	Glu	Ala	Phe	175	Thr	Glu	Gln	Glu	Leu	185
				185					190						195
Arg	Glu	Gln	Ala	185	Arg	Glu	Arg	Glu	190	Gly	Ala	Arg	Leu	Gln	200
				200					205						210
Leu	Ser	Ala	Ala	200	Thr	Ala	Glu	His	205	Ala	Arg	Leu	Gln	Ala	215
				215					220						225
Asp	Ala	Gln	Ala	215	Arg	Ala	Leu	Glu	220	Ala	Glu	Leu	Gln	Leu	230
				230					235						240
Glu	Ala	Pro	Gly	230	Pro	Pro	Ser	Pro	235	Met	Ala	Ser	Ala	Thr	245
				245					250						255
Leu	His	Gln	Asp	245	Leu	Ala	Val	Gln	250	Glu	Gln	Ser	Ala	Glu	260
				260					265						270
Gln	Gly	Ser	Leu	260	Ala	Leu	Val	Ser	265	Arg	Ala	Leu	Glu	Ala	270
				275					280						285

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Arg Ala Leu Gln Ala Gln Ala Gln Glu Leu Glu Glu Leu Asn Arg
 275 280
 Glu Leu Arg Gln Cys Asn Leu Gln Gln Phe Ile Gln Gln Thr Gly
 290 300
 Ala Ala Leu Pro Pro Pro Pro Arg Pro Asp Arg Gly Pro Pro Gly
 305 315
 Thr Gln Val Gly Val Val Leu Gly Gly Gly Trp Glu Val Arg Thr
 320 325 330
 Trp Pro Ser Pro Thr Pro Ser
 335

<210> 34

<211> 565

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1806850CD1

<400> 34

Met Lys Glu Glu Glu Glu Val Phe Gln Pro Met Leu Met Glu Tyr
 1 5 10 15
 Phe Thr Tyr Glu Glu Leu Lys Tyr Ile Lys Lys Val Ile Ala
 20 25 30
 Gln His Cys Ser Gln Lys Asp Thr Ala Glu Leu Leu Arg Gly Leu
 35 40 45
 Ser Leu Trp Asn His Ala Glu Glu Arg Gln Lys Phe Phe Lys Tyr
 50 55 60
 Ser Val Asp Glu Lys Ser Asp Lys Glu Ala Glu Val Ser Glu His
 65 70 75
 Ser Thr Gly Ile Thr His Leu Pro Pro Glu Val Met Leu Ser Ile
 80 85 90
 Phe Ser Tyr Leu Asn Pro Gln Glu Leu Cys Arg Cys Ser Gln Val
 95 100 105
 Ser Met Lys Trp Ser Gln Leu Thr Lys Thr Gly Ser Leu Trp Lys
 110 115 120
 His Leu Tyr Pro Val His Trp Ala Arg Gly Asp Trp Tyr Ser Gly
 125 130 135
 Pro Ala Thr Glu Leu Asp Thr Glu Pro Asp Asp Glu Trp Val Lys
 140 145 150
 Asn Arg Lys Asp Glu Ser Arg Ala Phe His Glu Trp Asp Glu Asp
 155 160 165
 Ala Asp Ile Asp Glu Ser Glu Glu Ser Ala Glu Glu Ser Ile Ala
 170 175 180
 Ile Ser Ile Ala Gln Met Glu Lys Arg Leu Leu His Gly Leu Ile
 185 190 195
 His Asn Val Leu Pro Tyr Val Gly Thr Ser Val Lys Thr Leu Val
 200 205 210
 Leu Ala Tyr Ser Ser Ala Val Ser Ser Lys Met Val Arg Gln Ile
 215 220 225
 Leu Glu Leu Cys Pro Asn Leu Glu His Leu Asp Leu Thr Gln Thr
 230 235 240
 Asp Ile Ser Asp Ser Ala Phe Asp Ser Trp Ser Trp Leu Gly Cys
 245 250 255
 Cys Gln Ser Leu Arg His Leu Asp Leu Ser Gly Cys Glu Lys Ile
 260 265 270
 Thr Asp Val Ala Leu Glu Lys Ile Ser Arg Ala Leu Gly Ile Leu
 275 280 285
 Thr Ser His Gln Ser Gly Phe Leu Lys Thr Ser Thr Ser Lys Ile
 290 295 300
 Thr Ser Thr Ala Trp Lys Asn Lys Asp Ile Thr Met Gln Ser Thr
 305 310 315
 Lys Gln Tyr Ala Cys Leu His Asp Leu Thr Asn Lys Gly Ile Gly

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Glu	Glu	Ile	Asp	320	Glu	His	Pro	Trp	325	Thr	Lys	Pro	Val	Ser	330
				335					340						345
Glu	Asn	Phe	Thr	350	Ser	Pro	Tyr	Val	355	Met	Leu	Asp	Ala	Glu	360
Leu	Ala	Asp	Ile	365	Glu	Asp	Thr	Val	370	Arg	His	Arg	Asn	Val	375
Glu	Ser	Leu	Cys	380	Val	Met	Glu	Thr	385	Ser	Asn	Phe	Ser	Cys	390
Thr	Ser	Gly	Cys	395	Phe	Ser	Lys	Asp	400	Ile	Val	Gly	Leu	Arg	395
Val	Cys	Trp	Gln	410	Gln	His	Cys	Ala	415	Ser	Pro	Ala	Phe	Ala	405
Gly	His	Ser	Phe	425	Cys	Cys	Thr	Gly	430	Ala	Leu	Arg	Thr	Met	420
Ser	Leu	Pro	Glu	440	Ser	Ser	Ala	Met	445	Cys	Arg	Lys	Ala	Ala	435
Arg	Leu	Pro	Arg	455	Gly	Lys	Asp	Leu	460	Ile	Tyr	Phe	Gly	Ser	440
Ser	Asp	Gln	Glu	470	Thr	Gly	Arg	Val	475	Leu	Leu	Phe	Leu	Ser	450
Gly	Cys	Tyr	Gln	485	Ile	Thr	Asp	His	490	Gly	Leu	Arg	Val	Leu	465
Gly	Gly	Gly	Leu	500	Pro	Tyr	Leu	Glu	505	His	Leu	Asn	Leu	Ser	480
Leu	Thr	Ile	Thr	515	Gly	Ala	Gly	Leu	520	Gln	Leu	Val	Ser	Ala	495
Pro	Ser	Leu	Asn	530	Asp	Glu	Tyr	Phe	535	Tyr	Tyr	Cys	Asp	Asn	510
Gly	Pro	His	Ala	545	Asp	Thr	Ala	Ser	550	Gly	Cys	Gln	Asn	Leu	525
Gly	Phe	Arg	Ala	560	Cys	Cys	Arg	Ser	565	Gly	Glu				540

<210> 35

<211> 228

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1851534CD1

<400> 35

Met	Asp	Phe	Ser	Phe	Ser	Phe	Met	Gln	Gly	Ile	Met	Gly	Asn	Thr	
1									10					15	
Ile	Gln	Gln	Pro	Pro	Gln	Leu	Ile	Asp	Ser	Ala	Asn	Ile	Arg	Gln	
					20				25					30	
Glu	Asp	Ala	Phe	Asp	Asn	Asn	Ser	Asp	Ile	Ala	Glu	Asp	Gly	Gly	
					35				40					45	
Gln	Thr	Pro	Tyr	Glu	Ala	Thr	Leu	Gln	Gln	Gly	Phe	Gln	Tyr	Pro	
					50				55					60	
Ala	Thr	Thr	Glu	Asp	Leu	Pro	Pro	Leu	Thr	Asn	Gly	Tyr	Pro	Ser	
					65				70					75	
Ser	Ile	Ser	Val	Tyr	Glu	Thr	Gln	Thr	Lys	Tyr	Gln	Ser	Tyr	Asn	
					80				85					90	
Gln	Tyr	Pro	Asn	Gly	Ser	Ala	Asn	Gly	Phe	Gly	Ala	Val	Arg	Asn	
					95				100					105	
Phe	Ser	Pro	Thr	Asp	Tyr	Tyr	His	Ser	Glu	Ile	Pro	Asn	Thr	Arg	
					110				115					120	
Pro	His	Glu	Ile	Leu	Glu	Lys	Pro	Ser	Pro	Pro	Gln	Pro	Pro	Pro	
					125				130					135	
Pro	Pro	Ser	Val	Pro	Gln	Thr	Val	Ile	Pro	Lys	Lys	Thr	Gly	Ser	
					140				145					150	

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Pro	Glu	Ile	Lys	Leu	Lys	Ile	Thr	Lys	Thr	Ile	Gln	Asn	Gly	Arg	
				155					160					165	
Glu	Leu	Phe	Glu	Ser	Ser	Leu	Cys	Gly	Asp	Leu	Leu	Asn	Glu	Val	
				170					175					180	
Gln	Ala	Ser	Glu	His	Thr	Lys	Ser	Lys	His	Glu	Ser	Arg	Lys	Glu	
				185					190					195	
Lys	Arg	Lys	Lys	Ser	Asn	Lys	His	Asp	Ser	Ser	Arg	Ser	Glu	Glu	
				200					205					210	
Arg	Lys	Ser	His	Lys	Ile	Pro	Lys	Leu	Glu	Pro	Glu	Glu	Gln	Asn	
				215					220					225	
Met	Thr	Lys													

<210> 36

<211> 495

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1868749CD1

<400> 36

Met	Lys	Gly	Met	Lys	Val	Glu	Val	Leu	Asn	Ser	Asp	Ala	Val	Leu	
				5					10					15	
Pro	Ser	Arg	Val	Tyr	Trp	Ile	Ala	Ser	Val	Ile	Gln	Thr	Ala	Gly	
				20					25					30	
Tyr	Arg	Val	Leu	Leu	Arg	Tyr	Glu	Gly	Phe	Glu	Asn	Asp	Ala	Ser	
				35					40					45	
His	Asp	Phe	Trp	Cys	Asn	Leu	Gly	Thr	Val	Asp	Val	His	Pro	Ile	
				50					55					60	
Gly	Trp	Cys	Ala	Ile	Asn	Ser	Lys	Ile	Leu	Val	Pro	Pro	Arg	Thr	
				65					70					75	
Ile	His	Ala	Lys	Phe	Thr	Asp	Trp	Lys	Gly	Tyr	Leu	Met	Lys	Arg	
				80					85					90	
Leu	Val	Gly	Ser	Arg	Thr	Leu	Pro	Val	Asp	Phe	His	Ile	Lys	Met	
				95					100					105	
Val	Glu	Ser	Met	Lys	Tyr	Pro	Phe	Arg	Gln	Gly	Met	Arg	Leu	Glu	
				110					115					120	
Val	Val	Asp	Lys	Ser	Gln	Val	Ser	Arg	Thr	Arg	Met	Ala	Val	Val	
				125					130					135	
Asp	Thr	Val	Ile	Gly	Gly	Arg	Leu	Arg	Leu	Leu	Tyr	Glu	Asp	Gly	
				140					145					150	
Asp	Ser	Asp	Asp	Asp	Phe	Trp	Cys	His	Met	Trp	Ser	Pro	Leu	Ile	
				155					160					165	
His	Pro	Val	Gly	Trp	Ser	Arg	Arg	Val	Gly	His	Gly	Ile	Lys	Met	
				170					175					180	
Ser	Glu	Arg	Arg	Ser	Asp	Met	Ala	His	His	Pro	Thr	Phe	Arg	Lys	
				185					190					195	
Ile	Tyr	Cys	Asp	Ala	Val	Pro	Tyr	Leu	Phe	Lys	Lys	Val	Arg	Ala	
				200					205					210	
Val	Tyr	Thr	Glu	Gly	Gly	Trp	Phe	Glu	Glu	Gly	Met	Lys	Leu	Glu	
				215					220					225	
Ala	Ile	Asp	Pro	Leu	Asn	Leu	Gly	Asn	Ile	Cys	Val	Ala	Thr	Val	
				230					235					240	
Cys	Lys	Val	Leu	Leu	Asp	Gly	Tyr	Leu	Met	Ile	Cys	Val	Asp	Gly	
				245					250					255	
Gly	Pro	Ser	Thr	Asp	Gly	Leu	Asp	Trp	Phe	Cys	Tyr	His	Ala	Ser	
				260					265					270	
Ser	His	Ala	Ile	Phe	Pro	Ala	Thr	Phe	Cys	Gln	Lys	Asn	Asp	Ile	
				275					280					285	
Glu	Leu	Thr	Pro	Pro	Lys	Gly	Tyr	Glu	Ala	Gln	Thr	Phe	Asn	Trp	
				290					295					300	
Glu	Asn	Tyr	Leu	Glu	Lys	Thr	Lys	Ser	Lys	Ala	Ala	Pro	Ser	Arg	

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Leu Phe Asn Met	305	310	315
Asp Cys Pro Asn His	320	Gly Phe Lys Val Gly Met	330
Lys Leu Glu Ala Val	335	Pro Arg Leu Ile Cys Val	345
Ala Thr Val Lys Arg	350	Leu Ser Ile His Phe	360
Asp Gly Trp Asp Ser	365	Trp Val Asp Cys Glu Ser	375
Pro Asp Ile Tyr Pro	380	Glu Leu Thr Gly Tyr Gln	390
Leu Gln Pro Pro Val	395	Ala Thr Pro Leu Lys Ala	405
Lys Glu Ala Thr Lys	410	Gln Phe Gly Lys Lys Arg	420
Lys Arg Ile Pro Pro	425	Pro Leu Arg Gln Gly Ser	435
Lys Lys Pro Leu Leu	440	Gln Gly Ala Arg Lys Ile	450
Ser Ser Glu Pro Val	455	Ile Ala Val Arg Val Lys	465
Glu Glu His Leu Asp	470	Asp Lys Ala Ser Ser Pro	480
Glu Leu Pro Val Ser	485	Lys Gln Glu Thr Asp Asp	495

<210> 37

<211> 1336

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1980010CD1

<400> 37

Met Val Asp Gln Leu	1	Glu Gln Ile Leu Ser	10	Val Ser Glu Leu Leu	15
Glu Lys His Gly Leu	5	Glu Lys Pro Ile Ser	20	Phe Val Lys Asn Thr	25
Gln Ser Ser Ser Glu	10	Glu Ala Arg Lys Leu	30	Met Val Arg Leu Thr	35
Arg His Thr Gly Arg	35	Lys Gln Pro Pro Val	40	Ser Glu Ser His Trp	45
Arg Thr Leu Leu Gln	50	Asp Met Leu Thr Met	55	Gln Gln Asn Val Tyr	60
Thr Cys Leu Asp Ser	65	Asp Ala Cys Tyr Glu	70	Ile Phe Thr Glu Ser	75
Leu Leu Cys Ser Ser	80	Arg Leu Glu Asn Ile	85	His Leu Ala Gly Gln	90
Met Met His Cys Ser	95	Ala Cys Ser Glu Asn	100	Pro Pro Ala Gly Ile	105
Ala His Lys Gly Asn	110	Pro His Tyr Arg Val	115	Ser Tyr Glu Lys Ser	120
Ile Asp Leu Val Leu	125	Ala Ala Ser Arg Glu	130	Tyr Phe Asn Ser Ser	135
Thr Asn Leu Thr Asp	140	Ser Cys Met Asp Leu	145	Ala Arg Cys Cys Leu	150
Gln Leu Ile Thr Asp	155	Arg Pro Pro Ala Ile	160	Gln Glu Glu Leu Asp	165
Leu Ile Gln Ala Val	170	Gly Cys Leu Glu Glu	175	Phe Gly Val Lys Ile	180
Leu Pro Leu Gln Val	185	Arg Leu Cys Pro Asp	190	Arg Ile Ser Leu Ile	195

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Lys Glu Cys Ile	200	Gln Ser Pro Thr	205	Tyr Lys Gln Ser	210
	215	Leu Ala Glu Leu Leu	220	Val Ala Gly Glu Asn	225
Lys Leu Leu Gly	230	Arg Gly Gln Val Leu	235	Leu Leu Val Glu Gln	240
Pro Glu Glu Arg	245	Ala Ser Met His Cys Gln	250		255
Ala Leu Arg Phe	260	Asp Tyr Lys Ala	265	Ser Trp Asp Val Cys Ser	270
Glu Leu Met Ala	275	Gly Tyr Pro Lys	280	Leu Ala Thr Arg Gln	300
Gln Leu Gly Gln	290	Ser Glu Gly Tyr Gln	295	Pro Pro Ser Ser Ile	315
Glu Leu Met Ala	305	Phe Ala Leu Thr His	310	Gln Thr Glu Ile Leu	330
Glu Leu Leu Leu	320	Ala Ser Ser Ser	325	Glu Gly Gly Glu Asn	345
Tyr Gln Arg Val	335	Asn Phe Gln Ile His	340	Val Gln Glu Asp Glu	360
Ile Ser Ala Ser	350	Pro Leu Thr Ser Lys	355	Leu Leu Arg Trp Thr	375
Val Gly Val Pro	365	Gly Ser Asn Ser Ala	370	Thr Thr Thr Thr	390
Thr Ala Thr Thr	380	Met Lys Val Leu Ser	385	Gln Trp Trp Lys Lys	405
Lys Ala Val Leu	395	Gln Ala Val Ser Asp	400	Gln Lys Cys Gly Gly	420
Ser Leu Thr Tyr	410	Leu Arg Pro Leu Gln	415	Asp Leu Glu Lys Gln	435
Ala Tyr Gln Ile	425	Gly Thr Thr Ala Asn	430	Ser Asn Pro Phe Val	450
Gly Cys His Pro	440	Phe Tyr Glu Ser Val	445	Gln His Val Pro Val	465
Ala Glu Ser Glu	455	Gly Thr Tyr Asp Thr	460	Gly Lys Leu Ala Glu	480
Glu Ser Phe Ala	470	Glu Val Phe Pro	475	Thr Thr Glu Val Leu Leu	495
Ala Lys Asn Lys	485	Gly Glu Val Phe Pro	490	Met Thr Leu Ala Leu	510
Gln Leu Ala Ser	500	Glu Ala Leu Pro Asn	505	Asp Ala Asn Arg Cys	525
Ala Tyr Leu Leu	515	Ala Leu Pro Gln Val	520	Ser Leu Gln Leu Ala Ala	540
Phe Glu Lys Gln	530	Ser Pro Ser Ala Leu	535	Leu Ala Pro Cys Phe	555
Tyr Tyr Tyr Ser	545	Leu Gln Ile Tyr Ala	550	Ala Asp Pro Lys Glu Leu	570
Arg Asp Lys Cys	560	His Pro Leu Tyr Arg	565	His Glu His Glu Ala	585
Ile Lys Met Val	575	Thr Arg His Val Thr	580	Gln Leu His Cys Tyr	600
Trp Pro Glu Asp	590	Leu Ile Ser Leu Thr	595	Gln Ile Leu Gln Gly	615
Asn Glu Arg Leu	605	Leu Asp Phe Thr Gln	610	Thr Ala Asp Asp Gln	630
Leu Arg Lys Gly	620	Val Asp Val Gln Arg	625	Glu Thr Leu Glu Glu	645
Tyr Lys Arg Glu	635	Thr Ile Leu Gly Leu	640	Gln Arg Tyr Ser Val	660
Ser Val Tyr Ser	650	Ile Ala Ile Ser Leu	655	Leu Glu Phe Leu Phe	675
Ser Arg Trp Glu	665	Val Phe Met Thr His	670		

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Asp Ser Gly Leu Ser Thr Leu Glu Ile Glu Asn Arg Ala Gln Asp 680 690
 Leu His Leu Phe Glu Thr Leu Lys Thr Asp Pro Glu Ala Phe His 695 700
 Gln His Met Val Lys Tyr Ile Tyr Pro Thr Ile Gly Gly Phe Asp 710 715
 His Glu Arg Leu Gln Tyr Tyr Phe Thr Leu Leu Glu Asn Cys Gly 720 725
 Cys Ala Asp Leu Gly Asn Cys Ala Ile Lys Pro Glu Thr His Ile 730 735
 Arg Leu Leu Lys Lys Phe Lys Val Val Ala Ser Gly Leu Asn Tyr 740 745
 Lys Lys Leu Thr Asp Glu Asn Met Ser Pro Leu Glu Ala Leu Glu 750 755
 Pro Val Leu Ser Ser Gln Asn Ile Leu Ser Ile Ser Lys Leu Val 760 765
 Pro Lys Ile Pro Glu Lys Asp Gly Gln Met Leu Ser Pro Ser Ser 770 775
 Leu Tyr Thr Ile Trp Leu Gln Lys Leu Phe Trp Thr Gly Asp Pro 780 785
 His Leu Ile Lys Gln Val Pro Gly Ser Ser Pro Glu Trp Leu His 790 795
 Ala Tyr Asp Val Cys Met Lys Tyr Phe Asp Arg Leu His Pro Gly 800 805
 Asp Leu Ile Thr Val Val Asp Ala Val Thr Phe Ser Pro Lys Ala 810 815
 Val Thr Lys Leu Ser Val Glu Ala Arg Lys Glu Met Thr Arg Lys 820 825
 Ala Ile Lys Thr Val Lys His Phe Ile Glu Lys Pro Arg Lys Arg 830 835
 Asn Ser Glu Asp Glu Ala Gln Glu Ala Lys Asp Ser Lys Val Thr 840 845
 Tyr Ala Asp Thr Leu Asn His Leu Glu Lys Ser Leu Ala His Leu 850 855
 Glu Thr Leu Ser His Ser Phe Ile Leu Ser Leu Lys Asn Ser Glu 860 865
 Gln Glu Thr Leu Gln Lys Tyr Ser His Leu Tyr Asp Leu Ser Arg 870 875
 Ser Glu Lys Glu Lys Leu His Asp Glu Ala Val Ala Ile Cys Leu 880 885
 Asp Gly Gln Pro Leu Ala Met Ile Gln Gln Leu Leu Glu Val Ala 890 895
 Val Gly Pro Leu Asp Ile Ser Pro Lys Asp Ile Val Gln Ser Ala 900 905
 Ile Met Lys Ile Ile Ser Ala Leu Ser Gly Gly Ser Ala Asp Leu 910 915
 Gly Gly Pro Arg Asp Pro Leu Lys Val Leu Glu Gly Val Val Ala 920 925
 Ala Val His Ala Ser Val Asp Lys Gly Glu Glu Leu Val Ser Pro 930 935
 Glu Asp Leu Leu Glu Trp Leu Arg Pro Phe Cys Ala Asp Asp Ala 940 945
 Trp Pro Val Arg Pro Arg Ile His Val Leu Gln Ile Leu Gly Gln 950 955
 Ser Phe His Leu Thr Glu Glu Asp Ser Lys Leu Leu Val Phe Phe 960 965
 Arg Thr Glu Ala Ile Leu Lys Ala Ser Trp Pro Gln Arg Gln Val 970 975
 Asp Ile Ala Asp Ile Glu Asn Glu Glu Asn Arg Tyr Cys Leu Phe 980 985
 Met Glu Leu Leu Glu Ser Ser His His Glu Ala Glu Phe Gln His 990 995
 Leu Val Leu Leu Leu Gln Ala Trp Pro Met Lys Ser Glu Tyr 1000 1005
 1010 1015
 1020 1025
 1030 1035
 1040 1045
 1050 1055
 1060 1065
 1070 1075
 1080 1085
 1090 1095
 1100 1105
 1110 1115
 1120 1125
 1130 1135
 1140 1145

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Val	Ile	Thr	Asn	Asn	Pro	Trp	Val	Arg	Leu	Ala	Thr	Val	Met	Leu	1145	1150	1155
Thr	Arg	Cys	Thr	Met	Glu	Asn	Lys	Glu	Gly	Leu	Gly	Asn	Glu	Val	1160	1165	1170
Leu	Lys	Met	Cys	Arg	Ser	Leu	Tyr	Asn	Thr	Lys	Gln	Met	Leu	Pro	1175	1180	1185
Ala	Glu	Gly	Val	Lys	Glu	Leu	Cys	Leu	Leu	Leu	Asn	Gln	Ser		1190	1195	1200
Leu	Leu	Leu	Pro	Ser	Leu	Lys	Leu	Leu	Leu	Glu	Ser	Arg	Asp	Glu	1205	1210	1215
His	Leu	His	Glu	Met	Ala	Leu	Glu	Gln	Ile	Thr	Ala	Val	Thr	Thr	1220	1225	1230
Val	Asn	Asp	Ser	Asn	Cys	Asp	Gln	Glu	Leu	Ser	Leu	Leu	Leu		1235	1240	1245
Asp	Ala	Lys	Leu	Leu	Val	Lys	Cys	Val	Ser	Thr	Pro	Phe	Tyr	Pro	1250	1255	1260
Arg	Ile	Val	Asp	His	Leu	Leu	Ala	Ser	Leu	Gln	Gln	Gly	Arg	Trp	1265	1270	1275
Asp	Ala	Glu	Glu	Leu	Gly	Arg	His	Leu	Arg	Glu	Ala	Gly	His	Glu	1280	1285	1290
Ala	Glu	Ala	Gly	Ser	Leu	Leu	Leu	Ala	Val	Arg	Gly	Thr	His	Gln	1295	1300	1305
Ala	Phe	Arg	Thr	Phe	Ser	Thr	Ala	Leu	Arg	Ala	Ala	Gln	His	Trp	1310	1315	1320
Val															1325	1330	1335

Val

<210> 38

<211> 934

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2259032CD1

<400> 38

Met	Phe	Trp	Lys	Phe	Asp	Leu	Asn	Thr	Thr	Ser	His	Val	Asp	Lys	1	5	10	15
Leu	Leu	Asp	Lys	Glu	His	Val	Thr	Leu	Gln	Glu	Leu	Met	Asp	Glu	20	25	30	
Asp	Asp	Ile	Leu	Gln	Glu	Cys	Lys	Ala	Gln	Asn	Gln	Lys	Leu	Leu	35	40	45	
Asp	Phe	Leu	Cys	Arg	Gln	Gln	Cys	Met	Glu	Glu	Leu	Val	Ser	Leu	50	55	60	
Ile	Thr	Gln	Asp	Pro	Pro	Leu	Asp	Met	Glu	Glu	Lys	Val	Arg	Phe	65	70	75	
Lys	Tyr	Pro	Asn	Thr	Ala	Cys	Glu	Leu	Leu	Thr	Cys	Asp	Val	Pro	80	85	90	
Gln	Ile	Ser	Asp	Arg	Leu	Gly	Gly	Asp	Glu	Ser	Leu	Leu	Ser	Leu	95	100	105	
Leu	Tyr	Asp	Phe	Leu	Asp	His	Glu	Pro	Pro	Leu	Asn	Pro	Leu	Leu	110	115	120	
Ala	Ser	Phe	Phe	Ser	Lys	Thr	Ile	Gly	Asn	Leu	Ile	Ala	Arg	Lys	125	130	135	
Thr	Glu	Gln	Val	Ile	Thr	Phe	Leu	Lys	Lys	Lys	Asp	Lys	Phe	Ile	140	145	150	
Ser	Leu	Val	Leu	Lys	His	Ile	Gly	Thr	Ser	Ala	Leu	Met	Asp	Leu	155	160	165	
Leu	Leu	Arg	Leu	Val	Ser	Cys	Val	Glu	Pro	Ala	Gly	Leu	Arg	Gln	170	175	180	
Asp	Val	Leu	His	Trp	Leu	Asn	Glu	Glu	Lys	Val	Ile	Gln	Arg	Leu	185	190	195	

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Val Glu Leu Ile His Pro Ser Gln Asp Glu Asp Arg Gln Ser Asn
 200 210
 Ala Ser Gln Thr Leu Cys Asp Ile Val Arg Leu Gly Arg Asp Gln
 215 225
 Gly Ser Gln Leu Gln Glu Ala Leu Glu Pro Asp Pro Leu Leu Thr
 230 240
 Ala Leu Glu Ser Arg Gln Asp Cys Val Glu Gln Leu Leu Lys Asn
 245 255
 Met Phe Asp Gly Asp Arg Thr Glu Ser Cys Leu Val Ser Gly Thr
 260 270
 Gln Val Leu Leu Thr Leu Leu Glu Thr Arg Arg Val Gly Thr Glu
 275 285
 Gly Leu Val Asp Ser Phe Ser Gln Gly Leu Glu Arg Ser Tyr Ala
 290 300
 Val Ser Ser Ser Val Leu His Gly Ile Glu Pro Arg Leu Lys Asp
 305 315
 Phe His Gln Leu Leu Leu Asn Pro Pro Lys Lys Lys Ala Ile Leu
 320 330
 Thr Thr Ile Gly Val Leu Glu Glu Pro Leu Gly Asn Ala Arg Leu
 335 345
 His Gly Ala Arg Leu Met Ala Ala Leu Leu His Thr Asn Thr Pro
 350 360
 Ser Ile Asn Gln Glu Leu Cys Arg Leu Asn Thr Met Asp Leu Leu
 365 375
 Leu Asp Leu Phe Phe Lys Tyr Thr Trp Asn Asn Phe Leu His Phe
 380 390
 Gln Val Glu Leu Cys Ile Ala Ala Ile Leu Ser His Ala Ala Arg
 395 405
 Glu Glu Arg Thr Glu Ala Ser Gly Ser Glu Ser Arg Val Glu Pro
 410 420
 Pro His Glu Asn Gly Asn Arg Ser Leu Glu Thr Pro Gln Pro Ala
 425 435
 Ala Ser Leu Pro Asp Asn Thr Met Val Thr His Leu Phe Gln Lys
 440 450
 Cys Cys Leu Val Gln Arg Ile Leu Glu Ala Trp Glu Ala Asn Asp
 455 465
 His Thr Gln Ala Ala Gly Gly Met Arg Arg Gly Asn Met Gly His
 470 480
 Leu Thr Arg Ile Ala Asn Ala Val Val Gln Asn Leu Glu Arg Gly
 485 495
 Pro Val Gln Thr His Ile Ser Glu Val Ile Arg Gly Leu Pro Ala
 500 510
 Asp Cys Arg Gly Arg Trp Glu Ser Phe Val Glu Glu Thr Leu Thr
 515 525
 Glu Thr Asn Arg Arg Asn Thr Val Asp Leu Ala Phe Ser Asp Tyr
 530 540
 Gln Ile Gln Gln Met Thr Ala Asn Phe Val Asp Gln Phe Gly Phe
 545 555
 Asn Asp Glu Glu Phe Ala Asp Gln Asp Asp Asn Ile Asn Ala Pro
 560 570
 Phe Asp Arg Ile Ala Glu Ile Asn Phe Asn Ile Asp Ala Asp Glu
 575 585
 Asp Ser Pro Ser Ala Ala Leu Phe Glu Ala Cys Cys Ser Asp Arg
 590 600
 Ile Gln Pro Phe Asp Asp Asp Glu Asp Glu Asp Ile Trp Glu Asp
 605 615
 Ser Asp Thr Arg Cys Ala Ala Arg Val Met Ala Arg Pro Arg Phe
 620 630
 Gly Ala Pro His Ala Ser Glu Ser Cys Ser Lys Asn Gly Pro Glu
 635 645
 Arg Gly Gly Gln Asp Gly Lys Ala Ser Leu Glu Ala His Arg Asp
 650 660
 Ala Pro Gly Ala Gly Ala Pro Pro Ala Pro Gly Lys Lys Glu Ala

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Pro	Pro	Val	Glu	665	Asp	Ser	Glu	Ala	670	Gly	Ala	Met	Trp	Thr	675
				680					685						690
Val	Phe	Asp	Glu	695	Pro	Ala	Asn	Ser	Thr	Pro	Thr	Ala	Pro	Gly	Val
				700											705
Val	Arg	Asp	Val	710	Gly	Ser	Ser	Val	Trp	Ala	Ala	Gly	Thr	Ser	Ala
				715											720
Pro	Glu	Glu	Lys	725	Gly	Trp	Ala	Lys	Phe	Thr	Asp	Phe	Gln	Pro	Phe
				730											735
Cys	Cys	Ser	Glu	740	Ser	Gly	Pro	Arg	Cys	Ser	Ser	Pro	Val	Asp	Thr
				745											750
Glu	Cys	Ser	His	755	Ala	Glu	Gly	Ser	Arg	Ser	Gln	Gly	Pro	Glu	Lys
				760											765
Ala	Phe	Ser	Pro	770	Ala	Ser	Pro	Cys	Ala	Trp	Asn	Val	Cys	Val	Thr
				775											780
Arg	Lys	Ala	Pro	785	Leu	Leu	Ala	Ser	Asp	Ser	Ser	Ser	Ser	Gly	Gly
				790											795
Ser	His	Ser	Glu	800	Asp	Gly	Asp	Gln	Lys	Ala	Ala	Ser	Ala	Met	Asp
				805											810
Ala	Val	Ser	Arg	815	Gly	Pro	Gly	Arg	Glu	Ala	Pro	Pro	Leu	Pro	Thr
				820											825
Val	Ala	Arg	Thr	830	Glu	Glu	Ala	Val	Gly	Arg	Val	Gly	Cys	Ala	Asp
				835											840
Ser	Arg	Leu	Leu	845	Ser	Pro	Ala	Cys	Pro	Ala	Pro	Lys	Glu	Val	Thr
				850											855
Ala	Ala	Pro	Ala	860	Val	Ala	Val	Pro	Pro	Glu	Ala	Thr	Val	Ala	Ile
				865											870
Thr	Thr	Ala	Leu	875	Ser	Lys	Ala	Gly	Pro	Ala	Ile	Pro	Thr	Pro	Ala
				880											885
Val	Ser	Ser	Ala	890	Leu	Ala	Val	Ala	Val	Pro	Leu	Gly	Pro	Ile	Met
				895											900
Ala	Val	Thr	Ala	905	Ala	Pro	Ala	Met	Val	Ala	Thr	Leu	Gly	Thr	Val
				910											915
Thr	Lys	Asp	Gly	920	Lys	Thr	Asp	Ala	Pro	Pro	Glu	Gly	Ala	Ala	Leu
				925											930
Asn	Gly	Pro	Val												

<210> 39

<211> 515

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2359526CD1

<400> 39

Met	Ala	Ala	Asn	Met	Tyr	Arg	Val	Gly	Asp	Tyr	Val	Tyr	Phe	Glu
				5					10					15
Asn	Ser	Ser	Ser	Asn	Pro	Tyr	Leu	Ile	Arg	Arg	Ile	Glu	Glu	Leu
				20					25					30
Asn	Lys	Thr	Ala	Ser	Gly	Asn	Val	Glu	Ala	Lys	Val	Val	Cys	Phe
				35					40					45
Tyr	Arg	Arg	Arg	Asp	Ile	Ser	Asn	Thr	Leu	Ile	Met	Leu	Ala	Asp
				50					55					60
Lys	His	Ala	Lys	Glu	Ile	Glu	Glu	Glu	Ser	Glu	Thr	Thr	Val	Glu
				65					70					75
Ala	Asp	Leu	Thr	Asp	Lys	Gln	Lys	His	Gln	Leu	Lys	His	Arg	Glu
				80					85					90
Leu	Phe	Leu	Ser	Arg	Gln	Tyr	Glu	Ser	Leu	Pro	Ala	Thr	His	Ile
				95					100					105
Arg	Gly	Lys	Cys	Ser	Val	Ala	Leu	Leu	Asn	Glu	Thr	Glu	Ser	Val
				110					115					120

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Leu Ser Tyr Leu Asp Lys Glu Asp Thr Phe Phe Tyr Ser Leu Val
125 135
Tyr Asp Pro Ser Leu Lys Thr Leu Leu Ala Asp Lys Gly Glu Ile
140 150
Arg Val Gly Pro Arg Tyr Gln Ala Asp Ile Pro Glu Met Leu Leu
155 165
Glu Gly Glu Ser Asp Glu Arg Glu Gln Ser Lys Leu Glu Val Lys
170 180
Val Trp Asp Pro Asn Ser Pro Leu Thr Asp Arg Gln Ile Asp Gln
185 195
Phe Leu Val Val Ala Arg Ala Val Gly Thr Phe Ala Arg Ala Leu
200 210
Asp Cys Ser Ser Ser Val Arg Gln Pro Ser Leu His Met Ser Ala
215 225
Ala Ala Ala Ser Arg Asp Ile Thr Leu Phe His Ala Met Asp Thr
230 240
Leu Tyr Arg His Ser Tyr Asp Leu Ser Ser Ala Ile Ser Val Leu
245 255
Val Pro Leu Gly Gly Pro Val Leu Cys Arg Asp Glu Met Glu Glu
260 270
Trp Ser Ala Ser Glu Ala Ser Leu Phe Glu Glu Ala Leu Glu Lys
275 285
Tyr Gly Lys Asp Phe Asn Asp Ile Arg Gln Asp Phe Leu Pro Trp
290 300
Lys Ser Leu Thr Ser Ile Ile Glu Tyr Tyr Tyr Met Trp Lys Thr
305 315
Thr Asp Arg Tyr Val Gln Gln Lys Arg Leu Lys Ala Ala Glu Ala
320 330
Glu Ser Lys Leu Lys Gln Val Tyr Ile Pro Thr Tyr Ser Lys Pro
335 345
Asn Pro Asn Gln Ile Ser Thr Ser Asn Gly Lys Pro Gly Ala Val
350 360
Asn Gly Ala Val Gly Thr Thr Phe Gln Pro Gln Asn Pro Leu Leu
365 375
Gly Arg Ala Cys Glu Ser Cys Tyr Ala Thr Gln Ser His Gln Trp
380 390
Tyr Ser Trp Gly Pro Pro Asn Met Gln Cys Arg Leu Cys Ala Ile
395 405
Cys Trp Leu Tyr Trp Lys Lys Tyr Gly Gly Leu Lys Met Pro Thr
410 420
Gln Ser Glu Glu Glu Lys Leu Ser Pro Ser Pro Thr Thr Glu Asp
425 435
Pro Arg Val Arg Ser His Val Ser Arg Gln Ala Met Gln Gly Met
440 450
Pro Val Arg Asn Thr Gly Ser Pro Lys Ser Ala Val Lys Thr Arg
455 465
Gln Ala Phe Phe Leu His Thr Thr Tyr Phe Thr Lys Phe Ala Arg
470 480
Gln Val Cys Lys Asn Thr Leu Arg Leu Arg Gln Ala Ala Arg Arg
485 495
Pro Phe Val Ala Ile Asn Tyr Ala Ala Ile Arg Ala Glu Cys Lys
500 510
Met Leu Leu Asn Ser
515

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<210> 40

<211> 146

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2456494CD1

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<400> 40
Met Val Asp Glu Leu Val Leu Leu Leu His Ala Leu Leu Met Arg
1 5 10 15
His Arg Ala Leu Ser Ile Glu Asn Ser Gln Leu Met Glu Gln Leu
20 25 30
Arg Leu Leu Val Cys Glu Arg Ala Ser Leu Arg Gln Val Arg
35 40 45
Pro Pro Ser Cys Pro Val Pro Phe Pro Glu Thr Phe Asn Gly Glu
50 55 60
Ser Ser Arg Leu Pro Glu Phe Ile Val Gln Thr Ala Ser Tyr Met
65 70 75
Leu Val Asn Glu Asn Arg Phe Cys Asn Asp Ala Met Lys Val Ala
80 85 90
Phe Leu Ile Ser Leu Leu Thr Gly Glu Ala Glu Glu Trp Val Val
95 100 105
Pro Tyr Ile Glu Met Asp Ser Pro Ile Leu Gly Asp Tyr Arg Ala
110 115 120
Phe Leu Asp Glu Met Lys Gln Cys Phe Gly Trp Asp Asp Asp Glu
125 130 135
Asp Asp Asp Asp Glu Glu Glu Glu Asp Asp Tyr
140 145

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<210> 41
<211> 580
<212> PRT
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte ID No: 2668536CD1

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<400> 41
Met Lys Glu Asn Lys Glu Asn Ser Ser Pro Ser Val Thr Ser Ala
1 5 10 15
Asn Leu Asp His Thr Lys Pro Cys Trp Tyr Trp Asp Lys Lys Asp
20 25 30
Leu Ala His Thr Pro Ser Gln Leu Glu Gly Leu Asp Pro Ala Thr
35 40 45
Glu Ala Arg Tyr Arg Arg Glu Gly Ala Arg Phe Ile Phe Asp Val
50 55 60
Gly Thr Arg Leu Gly Leu His Tyr Asp Thr Leu Ala Thr Gly Ile
65 70 75
Ile Tyr Phe His Arg Phe Tyr Met Phe His Ser Phe Lys Gln Phe
80 85 90
Pro Arg Tyr Val Thr Gly Ala Cys Cys Lys Phe Leu Ala Gly Lys
95 100 105
Val Glu Glu Thr Pro Lys Lys Cys Lys Asp Ile Ile Lys Thr Ala
110 115 120
Arg Ser Leu Leu Asn Asp Val Gln Phe Gly Gln Phe Gly Asp Asp
125 130 135
Pro Lys Glu Glu Val Met Val Leu Glu Arg Ile Leu Leu Gln Thr
140 145 150
Ile Lys Phe Asp Leu Gln Val Glu His Pro Tyr Gln Phe Leu Leu
155 160 165
Lys Tyr Ala Lys Gln Leu Lys Gly Asp Lys Asn Lys Ile Gln Lys
170 175 180
Leu Val Gln Met Ala Trp Thr Phe Val Asn Asp Ser Leu Cys Thr
185 190 195
Thr Leu Ser Leu Gln Trp Glu Pro Glu Ile Ile Ala Val Ala Val
200 205 210
Met Tyr Leu Ala Gly Arg Leu Cys Lys Phe Glu Ile Gln Glu Trp
215 220 225
Thr Ser Lys Pro Met Tyr Arg Arg Trp Trp Glu Gln Phe Val Gln
230 235 240

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Asp Val Pro Val Asp Val Leu Glu Asp Ile Cys His Gln Ile Leu
245 255
Asp Leu Tyr Ser Gln Gly Lys Gln Gln Met Pro His His Thr Pro
260 270
His Gln Leu Gln Gln Pro Pro Ser Leu Gln Pro Thr Pro Gln Val
275 285
Pro Gln Val Gln Gln Ser Gln Pro Ser Gln Ser Ser Glu Pro Ser
290 300
Gln Pro Gln Gln Lys Asp Pro Gln Gln Pro Ala Gln Gln Gln Gln
305 315
Pro Ala Gln Gln Pro Lys Lys Pro Ser Pro Gln Pro Ser Ser Pro
320 330
Arg Gln Val Lys Arg Ala Val Val Val Ser Pro Lys Glu Glu Asn
335 345
Lys Ala Ala Glu Pro Pro Pro Pro Lys Ile Pro Lys Ile Glu Thr
350 360
Thr His Pro Pro Leu Pro Pro Ala His Pro Pro Pro Asp Arg Lys
365 375
Pro Pro Leu Ala Ala Ala Leu Gly Glu Ala Glu Pro Pro Gly Pro
380 390
Val Asp Ala Thr Asp Leu Pro Lys Val Gln Ile Pro Pro Pro Ala
395 405
His Pro Ala Pro Val His Gln Pro Pro Pro Leu Pro His Arg Pro
410 420
Pro Pro Pro Pro Pro Ser Ser Tyr Met Thr Gly Met Ser Thr Thr
425 435
Ser Ser Tyr Met Ser Gly Glu Gly Tyr Gln Ser Leu Gln Ser Met
440 450
Met Lys Thr Glu Gly Pro Ser Tyr Gly Ala Leu Pro Pro Ala Tyr
455 465
Gly Pro Pro Ala His Leu Pro Tyr His Pro His Val Tyr Pro Pro
470 480
Asn Pro Pro Pro Pro Pro Val Pro Pro Pro Pro Ala Ser Phe Pro
485 495
His Leu Pro Ser His Pro Leu Leu Leu Ala Thr Pro Asn Pro His
500 510
Pro Pro Thr Thr Pro Thr Ser His Pro His Pro His Ala Ser Arg
515 525
Leu Pro Thr Gln Ser Pro Leu Ile Leu Leu Gln Gly Trp Ala Cys
530 540
Arg Gln Pro Ala Thr His Leu Leu Pro Ser Pro Leu Glu Asp Ser
545 555
Leu Leu Cys Pro Arg Pro Phe Pro His Pro Ala Cys Leu Gln Leu
560 570
Glu Gly Leu Gly Arg Ala Ala Trp Met Arg
575 580

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<210> 42

<211> 131

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2683225CD1

<400> 42

```

Met Ala Glu Pro Asp Tyr Ile Glu Asp Asp Asn Pro Glu Leu Ile
1 15
Arg Pro Gln Lys Leu Ile Asn Pro Val Lys Thr Ser Arg Asn His
20 30
Gln Asp Leu His Arg Glu Leu Leu Met Asn Gln Lys Arg Gly Leu
35 45
Ala Pro Gln Asn Lys Pro Glu Leu Gln Lys Val Met Glu Lys Arg

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Lys Arg Asp Gln Val Ile Lys Gln Lys Glu Glu Ala Gln Lys	50	55	60
	65	70	75
Lys Lys Ser Asp Leu Glu Ile Glu Leu Lys Arg Gln Gln Lys	80	85	90
Leu Glu Gln Leu Glu Lys Gln Lys Leu Gln Glu Glu Gln	95	100	105
Glu Asn Ala Pro Glu Phe Val Lys Val Lys Gly Asn Leu Arg Arg	110	115	120
Thr Gly Gln Glu Val Ala Gln Ala Gln Glu Ser	125	130	

<210> 43

<211> 812

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 2797839CD1

<400> 43

Met Gly Arg Lys Leu Asp Pro Thr Lys Glu Lys Arg Gly Pro Gly	1	5	10	15
Arg Lys Ala Arg Lys Gln Lys Gly Ala Glu Thr Glu Leu Val Arg	20	25	30	35
Phe Leu Pro Ala Val Ser Asp Glu Asn Ser Lys Arg Leu Ser Ser	40	45	50	55
Arg Ala Arg Lys Arg Ala Ala Lys Arg Arg Leu Gly Ser Val Glu	60	65	70	75
Ala Pro Lys Thr Asn Lys Ser Pro Glu Ala Lys Pro Leu Pro Gly	80	85	90	95
Lys Lys Gly Pro Gln Ser Leu Phe Asn Ala Pro Arg Gly Lys Lys	100	105	110	115
Arg Pro Ala Pro Gly Ser Asp Glu Glu Glu Glu Glu Asp Ser	120	125	130	135
Glu Glu Asp Gly Met Val Asn His Gly Asp Leu Trp Gly Ser Glu	140	145	150	155
Asp Asp Ala Asp Thr Val Asp Asp Tyr Gly Ala Asp Ser Asn Ser	160	165	170	175
Glu Asp Glu Glu Gly Glu Ala Leu Leu Pro Ile Glu Arg Ala	180	185	190	195
Ala Arg Lys Gln Lys Ala Arg Glu Ala Ala Gly Ile Gln Trp	200	205	210	215
Ser Glu Glu Glu Thr Glu Asp Glu Glu Glu Lys Glu Val Thr	220	225	230	235
Pro Glu Ser Gly Pro Pro Lys Val Glu Ala Asp Gly Gly Leu	240	245	250	255
Gln Ile Asn Val Asp Glu Glu Pro Phe Val Leu Pro Pro Ala Gly	260	265	270	275
Glu Met Glu Gln Asp Ala Gln Ala Pro Asp Leu Gln Arg Val His	280	285	290	295
Lys Arg Ile Gln Asp Ile Val Gly Ile Leu Arg Asp Phe Gly Ala	300	305	310	315
Gln Arg Glu Glu Gly Arg Ser Arg Ser Glu Tyr Leu Asn Arg Leu				
Lys Lys Asp Leu Ala Ile Tyr Tyr Ser Tyr Gly Asp Phe Leu Leu				
Gly Lys Leu Met Asp Leu Phe Pro Leu Ser Glu Leu Val Glu Phe				
Leu Glu Ala Asn Glu Val Pro Arg Pro Val Thr Leu Arg Thr Asn				

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Thr Leu Lys Thr Arg Arg Arg Asp Leu Ala Gln Ala Leu Ile Asn 320
 Arg Gly Val Asn Leu Asp Pro Leu Gly Lys Trp Ser Lys Thr Gly 330
 335
 Leu Val Val Tyr Asp Ser Ser Val Pro Ile Gly Ala Thr Pro Glu 340
 350
 Tyr Leu Ala Gly His Tyr Met Leu Gln Gly Ala Ser Ser Met Leu 355
 365
 Pro Val Met Ala Leu Ala Pro Gln Glu His Glu Arg Ile Leu Asp 370
 380
 Met Cys Cys Ala Pro Gly Gly Lys Thr Ser Tyr Met Ala Gln Leu 385
 395
 Met Lys Asn Thr Gly Val Ile Leu Ala Asn Asp Ala Asn Ala Glu 400
 410
 Arg Leu Lys Ser Val Val Gly Asn Leu His Arg Leu Gly Val Thr 415
 425
 Asn Thr Ile Ile Ser His Tyr Asp Gly Arg Gln Phe Pro Lys Val 430
 440
 Val Gly Gly Phe Asp Arg Val Leu Leu Asp Ala Pro Cys Ser Gly 445
 455
 Thr Gly Val Ile Ser Lys Asp Pro Ala Val Lys Thr Asn Lys Asp 460
 470
 Glu Lys Asp Ile Leu Arg Cys Ala His Leu Gln Lys Glu Leu Leu 465
 485
 Leu Ser Ala Ile Asp Ser Val Asn Ala Thr Ser Lys Thr Gly Gly 490
 500
 Tyr Leu Val Tyr Cys Thr Cys Ser Ile Thr Val Glu Glu Asn Glu 505
 515
 Trp Val Val Asp Tyr Ala Leu Lys Lys Arg Asn Val Arg Leu Val 520
 530
 Pro Thr Gly Leu Asp Phe Gly Gln Glu Gly Phe Thr Arg Phe Arg 535
 545
 Glu Arg Arg Phe His Pro Ser Leu Arg Ser Thr Arg Arg Phe Tyr 550
 560
 Pro His Thr His Asn Met Asp Gly Phe Phe Ile Ala Lys Phe Lys 565
 575
 Lys Phe Ser Asn Ser Ile Pro Gln Ser Gln Thr Gly Asn Ser Glu 580
 590
 Thr Ala Thr Pro Thr Asn Val Asp Leu Pro Gln Val Ile Pro Lys 595
 605
 Ser Glu Asn Ser Ser Gln Pro Ala Lys Lys Ala Lys Gly Ala Ala 610
 620
 Lys Thr Lys Gln Gln Leu Gln Lys Gln Gln His Pro Lys Lys Ala 625
 635
 Ser Phe Gln Lys Leu Asn Gly Ile Ser Lys Gly Ala Asp Ser Glu 640
 650
 Leu Ser Thr Val Pro Ser Val Thr Lys Thr Gln Ala Ser Ser Ser 655
 665
 Phe Gln Asp Ser Ser Gln Pro Ala Gly Lys Ala Glu Gly Ile Arg 670
 680
 Glu Pro Lys Val Thr Gly Lys Leu Lys Gln Arg Ser Pro Lys Leu 685
 695
 Gln Ser Ser Lys Lys Val Ala Phe Leu Arg Gln Asn Ala Pro Pro 700
 710
 Lys Gly Thr Asp Thr Gln Thr Pro Ala Val Leu Ser Pro Ser Lys 715
 725
 Thr Gln Ala Thr Leu Lys Pro Lys Asp His His Gln Pro Leu Gly 730
 740
 Arg Ala Lys Gly Val Glu Lys Gln Gln Leu Pro Glu Gln Pro Phe 745
 755
 Glu Lys Ala Ala Phe Gln Lys Gln Asn Asp Thr Pro Lys Gly Pro 760
 770
 Gln Pro Pro Thr Val Ser Pro Ile Arg Ser Ser Arg Pro Pro Pro 775

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Ala	Lys	Arg	Lys	785	Lys	Ser	Gln	Ser	Arg	790	Gly	Asn	Ser	Gln	Leu	795	Leu
				800						805						810	
Leu	Ser																

<210> 44
 <211> 537
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2959521CD1

<400> 44

Met	Arg	Gly	Val	Gly	Ala	Arg	Val	Tyr	Ala	Asp	Ala	Pro	Ala	Lys			
1				5					10					15			
Leu	Leu	Leu	Pro	Pro	Pro	Ala	Ala	Trp	Asp	Leu	Ala	Val	Arg	Leu			
				20					25					30			
Arg	Gly	Ala	Glu	Ala	Ala	Ser	Glu	Arg	Gln	Val	Tyr	Ser	Val	Thr			
				35					40					45			
Met	Lys	Leu	Leu	Leu	Leu	His	Pro	Ala	Phe	Gln	Ser	Cys	Leu	Leu			
				50					55					60			
Leu	Thr	Leu	Leu	Gly	Leu	Trp	Arg	Thr	Thr	Pro	Glu	Ala	His	Ala			
				65					70					75			
Ser	Ser	Leu	Gly	Ala	Pro	Ala	Ile	Ser	Ala	Ala	Ser	Phe	Leu	Gln			
				80					85					90			
Asp	Leu	Ile	His	Arg	Tyr	Gly	Glu	Gly	Asp	Ser	Leu	Thr	Leu	Gln			
				95					100					105			
Gln	Leu	Lys	Ala	Leu	Leu	Asn	His	Leu	Asp	Val	Gly	Val	Gly	Arg			
				110					115					120			
Gly	Asn	Val	Thr	Gln	His	Val	Gln	Gly	His	Arg	Asn	Leu	Ser	Thr			
				125					130					135			
Cys	Phe	Ser	Ser	Gly	Asp	Leu	Phe	Thr	Ala	His	Asn	Phe	Ser	Glu			
				140					145					150			
Gln	Ser	Arg	Ile	Gly	Ser	Ser	Glu	Leu	Gln	Glu	Phe	Cys	Pro	Thr			
				155					160					165			
Ile	Leu	Gln	Gln	Leu	Asp	Ser	Arg	Ala	Cys	Thr	Ser	Glu	Asn	Gln			
				170					175					180			
Glu	Asn	Glu	Glu	Asn	Glu	Gln	Thr	Glu	Glu	Gly	Arg	Pro	Ser	Ala			
				185					190					195			
Val	Glu	Val	Trp	Gly	Tyr	Gly	Leu	Leu	Cys	Val	Thr	Val	Ile	Ser			
				200					205					210			
Leu	Cys	Ser	Leu	Leu	Gly	Ala	Ser	Val	Val	Pro	Phe	Met	Lys	Lys			
				215					220					225			
Thr	Phe	Tyr	Lys	Arg	Leu	Leu	Leu	Tyr	Phe	Ile	Ala	Leu	Ala	Ile			
				230					235					240			
Gly	Thr	Leu	Tyr	Ser	Asn	Ala	Leu	Phe	Gln	Leu	Ile	Pro	Glu	Ala			
				245					250					255			
Phe	Gly	Phe	Asn	Pro	Leu	Glu	Asp	Tyr	Tyr	Val	Ser	Lys	Ser	Ala			
				260					265					270			
Val	Val	Phe	Gly	Gly	Phe	Tyr	Leu	Phe	Phe	Phe	Thr	Glu	Lys	Ile			
				275					280					285			
Leu	Lys	Ile	Leu	Leu	Lys	Gln	Lys	Asn	Glu	His	His	His	Gly	His			
				290					295					300			
Ser	His	Tyr	Ala	Ser	Glu	Ser	Leu	Pro	Ser	Lys	Lys	Asp	Gln	Glu			
				305					310					315			
Glu	Gly	Val	Met	Glu	Lys	Leu	Gln	Asn	Gly	Asp	Leu	Asp	His	Met			
				320					325					330			
Ile	Pro	Gln	His	Cys	Ser	Ser	Glu	Leu	Asp	Gly	Lys	Ala	Pro	Met			
				335					340					345			
Val	Asp	Glu	Lys	Val	Ile	Val	Gly	Ser	Leu	Ser	Val	Gln	Asp	Leu			
				350					355					360			

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Gln Ala Ser Gln Ser Ala Cys Tyr Trp Leu Lys Gly Val Arg Tyr
 365 370
 Ser Asp Ile Gly Thr Leu Ala Trp Met Ile Thr Leu Ser Asp Gly
 380 385
 Leu His Asn Phe Ile Asp Gly Leu Ala Ile Gly Ala Ser Phe Thr
 395 400
 Val Ser Val Phe Gln Gly Ile Ser Thr Ser Val Ala Ile Leu Cys
 410 415
 Glu Glu Phe Pro His Glu Leu Gly Asp Phe Val Ile Leu Leu Asn
 425 430
 Ala Gly Met Ser Ile Gln Gln Ala Leu Phe Phe Asn Phe Leu Ser
 440 445
 Ala Cys Cys Cys Tyr Leu Gly Leu Ala Phe Gly Ile Leu Ala Gly
 455 460
 Ser His Phe Ser Ala Asn Trp Ile Phe Ala Leu Ala Gly Gly Met
 470 475
 Phe Leu Tyr Ile Ser Leu Ala Asp Met Phe Pro Glu Met Asn Glu
 485 490
 Val Cys Gln Glu Asp Glu Arg Lys Gly Ser Ile Leu Ile Pro Phe
 500 505
 Ile Ile Gln Asn Leu Gly Leu Leu Thr Gly Phe Thr Ile Met Val
 515 520
 Val Leu Thr Met Tyr Ser Gly Gln Ile Gln Ile Gly
 530 535

<210> 45

<211> 584

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 3082014CD1

<400> 45

Met Leu Trp Gly Gly Arg Val Gly Leu Thr Gly Val Phe Gln Ser
 1 5 10
 Leu Ser Tyr Arg Gly Lys Cys Ser Val Thr Leu Leu Asn Glu Thr
 20 25
 Asp Ile Leu Ser Gln Tyr Leu Glu Lys Glu Asp Cys Phe Phe Tyr
 35 40
 Ser Leu Val Phe Asp Pro Val Gln Lys Thr Leu Leu Ala Asp Gln
 50 55
 Gly Glu Ile Arg Val Gly Cys Lys Tyr Gln Ala Glu Ile Pro Asp
 65 70
 Arg Leu Val Glu Gly Glu Ser Asp Asn Arg Asn Gln Gln Lys Met
 80 85
 Glu Met Lys Val Trp Asp Pro Asp Asn Pro Leu Thr Asp Arg Gln
 95 100
 Ile Asp Gln Phe Leu Val Val Ala Arg Ala Val Gly Thr Phe Ala
 110 115
 Arg Ala Leu Asp Cys Ser Ser Ser Ile Arg Gln Pro Ser Leu His
 125 130
 Met Ser Ala Ala Ala Ser Arg Asp Ile Thr Leu Phe His Ala
 140 145
 Met Asp Thr Leu Gln Arg Asn Gly Tyr Asp Leu Ala Lys Ala Met
 155 160
 Ser Thr Leu Val Pro Gln Gly Gly Pro Val Leu Cys Arg Asp Glu
 170 175
 Met Glu Glu Trp Ser Ala Ser Glu Ala Met Leu Phe Glu Glu Ala
 185 190
 Leu Glu Lys Tyr Gly Lys Asp Phe Asn Asp Ile Arg Gln Asp Phe
 200 205
 Leu Pro Trp Lys Ser Leu Ala Ser Ile Val Gln Phe Tyr Tyr Met
 210 215

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Trp Lys Thr Thr	215	220	225
Asp Arg Tyr Ile Gln Gln Lys Arg Leu Lys	230	235	240
Ala Glu Ala Asp Ser Lys Leu Lys Gln Val Tyr Ile Pro Thr Tyr	245	250	255
Thr Lys Pro Asn Pro Asn Gln Ile Ile Ser Val Gly Ser Lys Pro	260	265	270
Gly Met Asn Gly Ala Gly Phe Gln Lys Gly Leu Thr Cys Glu Ser	275	280	285
Cys His Thr Thr Gln Ser Ala Gln Trp Tyr Ala Trp Gly Pro Pro	290	295	300
Asn Met Gln Cys Arg Leu Cys Ala Ser Cys Trp Ile Tyr Trp Lys	305	310	315
Lys Tyr Gly Gly Leu Lys Thr Pro Thr Gln Leu Glu Gly Ala Thr	320	325	330
Arg Gly Thr Thr Glu Pro His Ser Arg Gly His Leu Ser Arg Pro	335	340	345
Glu Ala Gln Ser Leu Ser Pro Tyr Thr Thr Ser Ala Asn Arg Ala	350	355	360
Lys Leu Leu Ala Lys Asn Arg Gln Thr Phe Leu Leu Gln Thr Thr	365	370	375
Lys Leu Thr Arg Leu Ala Arg Arg Met Cys Arg Asp Leu Leu Gln	380	385	390
Pro Arg Arg Ala Ala Arg Arg Pro Tyr Ala Pro Ile Asn Ala Asn	395	400	405
Ala Ile Lys Ala Glu Cys Ser Ile Arg Leu Pro Lys Ala Ala Lys	410	415	420
Thr Pro Leu Lys Ile His Pro Leu Val Arg Leu Pro Leu Ala Thr	425	430	435
Ile Val Lys Asp Leu Val Ala Gln Ala Pro Leu Lys Pro Lys Thr	440	445	450
Pro Arg Gly Thr Lys Thr Pro Ile Asn Arg Asn Gln Leu Ser Gln	455	460	465
Asn Arg Gly Leu Gly Gly Ile Met Val Lys Arg Ala Tyr Glu Thr	470	475	480
Met Ala Gly Ala Gly Val Pro Phe Ser Ala Asn Gly Arg Pro Leu	485	490	495
Ala Ser Gly Ile Arg Ser Ser Ser Gln Pro Ala Ala Lys Arg Gln	500	505	510
Lys Leu Asn Pro Ala Asp Ala Pro Asn Pro Val Val Phe Val Ala	515	520	525
Thr Lys Asp Thr Arg Ala Leu Arg Lys Ala Leu Thr His Leu Glu	530	535	540
Met Arg Arg Ala Ala Arg Arg Pro Asn Leu Pro Leu Lys Val Lys	545	550	555
Pro Thr Leu Ile Ala Val Arg Pro Pro Val Pro Leu Pro Ala Pro	560	565	570
Ser His Pro Ala Ser Thr Asn Glu Pro Ile Val Leu Glu Asp	575	580	

<210> 46

<211> 425

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 3520701CD1

<400> 46

Met Ala Gly Ala Glu Gly Ala Ala Gly Arg Gln Ser Glu Leu Glu	1	5	10	15
Pro Val Val Ser Leu Val Asp Val Leu Glu Glu Asp Glu Glu Leu	20	25	30	

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Glu Asn Glu Ala Cys Ala Val Leu Gly Gly Ser Asp Ser Glu Lys
 35 45
 Cys Ser Tyr Ser Gln Gly Ser Val Lys Arg Gln Ala Leu Tyr Ala
 50 60
 Cys Ser Thr Cys Thr Pro Glu Gly Glu Glu Pro Ala Gly Ile Cys
 65 75
 Leu Ala Cys Ser Tyr Glu Cys His Gly Ser His Lys Leu Phe Glu
 80 90
 Leu Tyr Thr Lys Arg Asn Phe Arg Cys Asp Cys Gly Asn Ser Lys
 95 105
 Phe Lys Asn Leu Glu Cys Lys Leu Leu Pro Asp Lys Ala Lys Val
 110 120
 Asn Ser Gly Asn Lys Tyr Asn Asp Asn Phe Phe Gly Leu Tyr Cys
 125 135
 Ile Cys Lys Arg Pro Tyr Pro Asp Pro Glu Asp Glu Ile Pro Asp
 140 150
 Glu Met Ile Gln Cys Val Val Cys Glu Asp Trp Phe His Gly Arg
 155 165
 His Leu Gly Ala Ile Pro Pro Glu Ser Gly Asp Phe Gln Glu Met
 170 180
 Val Cys Gln Ala Cys Met Lys Arg Cys Ser Phe Leu Trp Ala Tyr
 185 195
 Ala Ala Gln Leu Ala Val Thr Lys Ile Ser Thr Glu Asp Asp Gly
 200 210
 Leu Val Arg Asn Ile Asp Gly Ile Gly Asp Gln Glu Val Ile Lys
 215 225
 Pro Glu Asn Gly Glu His Gln Asp Ser Thr Leu Lys Glu Asp Val
 230 240
 Pro Glu Gln Gly Lys Asp Asp Val Arg Glu Val Lys Val Glu Gln
 245 255
 Asn Ser Glu Pro Cys Ala Gly Ser Ser Ser Glu Ser Asp Leu Gln
 260 270
 Thr Val Phe Lys Asn Glu Ser Leu Asn Ala Glu Ser Lys Ser Gly
 275 285
 Cys Lys Leu Gln Glu Leu Lys Ala Lys Gln Leu Ile Lys Lys Asp
 290 300
 Thr Ala Thr Tyr Trp Pro Leu Asn Trp Arg Ser Lys Leu Cys Thr
 305 315
 Cys Gln Asp Cys Met Lys Met Tyr Gly Asp Leu Asp Val Leu Phe
 320 330
 Leu Thr Asp Glu Tyr Asp Thr Val Leu Ala Tyr Glu Asn Lys Gly
 335 345
 Lys Ile Ala Gln Ala Thr Asp Arg Ser Asp Pro Leu Met Asp Thr
 350 360
 Leu Ser Ser Met Asn Arg Val Gln Gln Val Glu Leu Ile Cys Glu
 365 375
 Tyr Asn Asp Leu Lys Thr Glu Leu Lys Asp Tyr Leu Lys Arg Phe
 380 390
 Ala Asp Glu Gly Thr Val Val Lys Arg Glu Asp Ile Gln Gln Phe
 395 405
 Phe Glu Glu Phe Gln Ser Lys Lys Arg Arg Arg Val Asp Gly Met
 410 415 420
 Gln Tyr Tyr Cys Ser
 425

<210> 47
 <211> 255
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 4184320CD1

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<400> 47

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Met Tyr Val Arg Val Ser Phe Asp Thr Lys Pro Asp Leu Leu Leu
 1          5          10          15
His Leu Met Thr Lys Glu Trp Gln Leu Glu Leu Pro Lys Leu Leu
          20          25          30
Ile Ser Val His Gly Gly Leu Gln Asn Phe Glu Leu Gln Pro Lys
          35          40          45
Leu Lys Gln Val Phe Gly Lys Gly Leu Ile Lys Ala Ala Met Thr
          50          55          60
Thr Gly Ala Trp Ile Phe Thr Gly Gly Val Asn Thr Gly Val Ile
          65          70          75
Arg His Val Gly Asp Ala Leu Lys Asp His Ala Ser Lys Ser Arg
          80          85          90
Gly Lys Ile Cys Thr Ile Gly Ile Ala Pro Trp Gly Ile Val Glu
          95          100          105
Asn Gln Glu Asp Leu Ile Gly Arg Asp Val Val Arg Pro Tyr Gln
          110          115          120
Thr Met Ser Asn Pro Met Ser Lys Leu Thr Val Leu Asn Ser Met
          125          130          135
His Ser His Phe Ile Leu Ala Asp Asn Gly Thr Thr Gly Lys Tyr
          140          145          150
Gly Ala Glu Val Lys Leu Arg Arg Gln Leu Glu Lys His Ile Ser
          155          160          165
Leu Gln Lys Ile Asn Thr Arg Cys Leu Pro Phe Phe Ser Leu Asp
          170          175          180
Ser Arg Leu Phe Tyr Ser Phe Trp Gly Ser Cys Gln Leu Asp Ser
          185          190          195
Val Gly Ile Gly Gln Gly Val Pro Val Val Ala Leu Ile Val Glu
          200          205          210
Gly Gly Pro Asn Val Ile Ser Ile Val Leu Glu Tyr Leu Arg Asp
          215          220          225
Thr Pro Pro Val Pro Val Val Val Cys Asp Gly Ser Gly Arg Ala
          230          235          240
Ser Asp Ile Leu Ala Phe Gly His Lys Tyr Ser Glu Glu Gly Gly
          245          250          255

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<210> 48

<211> 111

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 4764233CD1

<400> 48

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Met Ser Trp Arg Gly Arg Ser Thr Tyr Arg Pro Arg Pro Arg Arg
 1          5          10          15
Ser Leu Gln Pro Pro Glu Leu Ile Gly Ala Met Leu Glu Pro Thr
          20          25          30
Asp Glu Glu Pro Lys Glu Glu Lys Pro Pro Thr Lys Ser Arg Asn
          35          40          45
Pro Thr Pro Asp Gln Lys Arg Glu Asp Asp Gln Gly Ala Ala Glu
          50          55          60
Ile Gln Val Pro Asp Leu Glu Ala Asp Leu Gln Glu Leu Cys Gln
          65          70          75
Thr Lys Thr Gly Asp Gly Cys Glu Gly Gly Thr Asp Val Lys Gly
          80          85          90
Lys Ile Leu Pro Lys Ala Glu His Phe Lys Met Pro Glu Ala Gly
          95          100          105
Glu Gly Lys Ser Gln Val
          110

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<210> 49

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<211> 422

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 4817352CD1

<400> 49

Met	Gly	Lys	Ala	Lys	Val	Pro	Ala	Ser	Lys	Arg	Ala	Pro	Ser	Ser	
1					5				10					15	
Pro	Val	Ala	Lys	Pro	Gly	Pro	Val	Lys	Thr	Leu	Thr	Arg	Lys	Lys	
				20					25					30	
Asn	Lys	Lys	Lys	Lys	Arg	Phe	Trp	Lys	Ser	Lys	Ala	Arg	Glu	Val	
				35					40					45	
Ser	Lys	Lys	Pro	Ala	Ser	Gly	Pro	Gly	Ala	Val	Val	Arg	Pro	Pro	
				50					55					60	
Lys	Ala	Pro	Glu	Asp	Phe	Ser	Gln	Asn	Trp	Lys	Ala	Leu	Gln	Glu	
				65					70					75	
Trp	Leu	Leu	Lys	Gln	Lys	Ser	Gln	Ala	Pro	Glu	Lys	Pro	Leu	Val	
				80					85					90	
Ile	Ser	Gln	Met	Gly	Ser	Lys	Lys	Lys	Pro	Lys	Ile	Ile	Gln	Gln	
				95					100					105	
Asn	Lys	Lys	Glu	Thr	Ser	Pro	Gln	Val	Lys	Gly	Glu	Glu	Met	Pro	
				110					115					120	
Ala	Gly	Lys	Asp	Gln	Glu	Ala	Ser	Arg	Gly	Ser	Val	Pro	Ser	Gly	
				125					130					135	
Ser	Lys	Met	Asp	Arg	Arg	Ala	Pro	Val	Pro	Arg	Thr	Lys	Ala	Ser	
				140					145					150	
Gly	Thr	Glu	His	Asn	Lys	Lys	Gly	Thr	Lys	Glu	Arg	Thr	Asn	Gly	
				155					160					165	
Asp	Ile	Val	Pro	Glu	Arg	Gly	Asp	Ile	Lys	His	Lys	Lys	Arg	Lys	
				170					175					180	
Ala	Lys	Glu	Ala	Ala	Pro	Ala	Pro	Pro	Thr	Glu	Glu	Asp	Ile	Trp	
				185					190					195	
Phe	Asp	Asp	Val	Asp	Pro	Ala	Asp	Ile	Glu	Ala	Ala	Ile	Gly	Pro	
				200					205					210	
Glu	Ala	Ala	Lys	Ile	Ala	Arg	Lys	Gln	Leu	Gly	Gln	Ser	Glu	Gly	
				215					220					225	
Ser	Val	Ser	Leu	Ser	Leu	Val	Lys	Glu	Gln	Ala	Phe	Gly	Gly	Leu	
				230					235					240	
Thr	Arg	Ala	Leu	Ala	Leu	Asp	Cys	Glu	Met	Val	Gly	Val	Gly	Pro	
				245					250					255	
Lys	Gly	Glu	Glu	Ser	Met	Ala	Ala	Arg	Val	Ser	Ile	Val	Asn	Gln	
				260					265					270	
Tyr	Gly	Lys	Cys	Val	Tyr	Asp	Lys	Tyr	Val	Lys	Pro	Thr	Glu	Pro	
				275					280					285	
Val	Thr	Asp	Tyr	Arg	Thr	Ala	Val	Ser	Gly	Ile	Arg	Pro	Glu	Asn	
				290					295					300	
Leu	Lys	Gln	Gly	Glu	Glu	Leu	Glu	Val	Val	Gln	Lys	Glu	Val	Ala	
				305					310					315	
Glu	Met	Leu	Lys	Gly	Arg	Ile	Leu	Val	Gly	His	Ala	Leu	His	Asn	
				320					325					330	
Asp	Leu	Lys	Val	Leu	Phe	Leu	Asp	His	Pro	Lys	Lys	Lys	Ile	Arg	
				335					340					345	
Asp	Thr	Gln	Lys	Tyr	Lys	Pro	Phe	Lys	Ser	Gln	Val	Lys	Ser	Gly	
				350					355					360	
Arg	Pro	Ser	Leu	Arg	Leu	Leu	Ser	Glu	Lys	Ile	Leu	Gly	Leu	Gln	
				365					370					375	
Val	Gln	Gln	Ala	Glu	His	Cys	Ser	Ile	Gln	Asp	Ala	Gln	Ala	Ala	
				380					385					390	
Met	Arg	Leu	Tyr	Val	Met	Val	Lys	Lys	Glu	Trp	Glu	Ser	Met	Ala	
				395					400					405	

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Arg Asp Arg Arg Pro Leu Leu Thr Ala Pro Asp His Cys Ser Asp
 410 415 420

Asp Ala

<210> 50

<211> 397

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5040573CD1

<400> 50

Met Ala Met Ile Glu Leu Gly Phe Gly Arg Gln Asn Phe His Pro
 1 5 10 15
 Leu Lys Arg Lys Ser Ser Leu Leu Leu Lys Leu Ile Ala Val Val
 20 25 30
 Phe Ala Val Leu Leu Phe Cys Glu Phe Leu Ile Tyr Tyr Leu Ala
 35 40 45
 Ile Phe Gln Cys Asn Trp Pro Glu Val Lys Thr Thr Ala Ser Asp
 50 55 60
 Gly Glu Gln Thr Thr Arg Glu Pro Val Leu Lys Ala Met Phe Leu
 65 70 75
 Ala Asp Thr His Leu Leu Gly Glu Phe Leu Gly His Trp Leu Asp
 80 85 90
 Lys Leu Arg Arg Glu Trp Gln Met Glu Arg Ala Phe Gln Thr Ala
 95 100 105
 Leu Trp Leu Leu Gln Pro Glu Val Val Phe Ile Leu Gly Asp Ile
 110 115 120
 Phe Asp Glu Gly Lys Trp Ser Thr Pro Glu Ala Trp Ala Asp Asp
 125 130 135
 Val Glu Arg Phe Gln Lys Met Phe Arg His Pro Ser His Val Gln
 140 145 150
 Leu Lys Val Val Ala Gly Asn His Asp Ile Gly Phe His Tyr Glu
 155 160 165
 Met Asn Thr Tyr Lys Val Glu Arg Phe Glu Lys Val Phe Ser Ser
 170 175 180
 Glu Arg Leu Phe Ser Trp Lys Gly Ile Asn Phe Val Met Val Asn
 185 190 195
 Ser Val Ala Leu Asn Gly Asp Gly Cys Gly Ile Cys Ser Glu Thr
 200 205 210
 Glu Ala Glu Leu Ile Glu Val Ser His Arg Leu Asn Cys Ser Arg
 215 220 225
 Glu Gln Ala Arg Gly Ser Ser Arg Cys Gly Pro Gly Pro Leu Leu
 230 235 240
 Pro Thr Ser Ala Pro Val Leu Leu Gln His Tyr Pro Leu Tyr Arg
 245 250 255
 Arg Ser Asp Ala Asn Cys Ser Gly Glu Asp Ala Ala Pro Pro Glu
 260 265 270
 Glu Arg Asp Ile Pro Phe Lys Glu Asn Tyr Asp Val Leu Ser Arg
 275 280 285
 Glu Ala Ser Gln Lys Leu Leu Trp Trp Leu Gln Pro Arg Leu Val
 290 295 300
 Leu Ser Gly His Thr His Ser Ala Cys Glu Val His His Gly Gly
 305 310 315
 Arg Val Pro Glu Leu Ser Val Pro Ser Phe Ser Trp Arg Asn Arg
 320 325 330
 Asn Asn Pro Ser Phe Ile Met Gly Ser Ile Thr Pro Thr Asp Tyr
 335 340 345
 Thr Leu Ser Lys Cys Tyr Leu Pro Arg Glu Asp Val Val Leu Ile
 350 355 360
 Ile Tyr Cys Gly Val Val Gly Phe Leu Val Val Leu Thr Leu Thr

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His Phe Gly Leu	365	Leu Ala Ser Pro Phe	370	Leu Ser Gly Leu Asn	375
	380		385		390
Leu Gly Lys Arg	395	Lys Thr Arg			

<210> 51

<211> 800

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5627029CD1

<400> 51

Met Gly Ser Ser Lys Lys His Arg Gly Glu Lys Glu Ala Ala Gly	1	5	10	15
Thr Thr Ala Ala Ala Gly Thr Gly Gly Ala Thr Glu Gln Pro Pro	20	25	30	35
Arg His Arg Glu His Lys Lys His Lys His Arg Ser Gly Gly Ser	40	45	50	55
Gly Gly Ser Gly Gly Glu Arg Arg Lys Arg Ser Arg Glu Arg Gly	60	65	70	75
Gly Glu Arg Gly Ser Gly Arg Arg Gly Ala Glu Ala Glu Ala Arg	80	85	90	95
Ser Ser Thr His Gly Arg Glu Arg Ser Gln Ala Glu Pro Ser Glu	100	105	110	115
Arg Arg Val Lys Arg Glu Lys Arg Asp Asp Gly Tyr Glu Ala Ala	120	125	130	135
Ala Ser Ser Lys Thr Ser Ser Gly Asp Ala Ser Ser Leu Ser Ile	140	145	150	155
Glu Glu Thr Asn Lys Leu Arg Ala Lys Lys Gly Leu Lys Pro Leu	160	165	170	175
Glu Val Asn Ala Ile Lys Lys Glu Ala Gly Thr Lys Glu Glu Pro	180	185	190	195
Val Thr Ala Asp Val Ile Asn Pro Met Ala Leu Arg Gln Arg Glu	200	205	210	215
Glu Leu Arg Glu Lys Leu Ala Ala Ala Lys Glu Lys Arg Leu Leu	220	225	230	235
Asn Gln Lys Leu Gly Lys Ile Lys Thr Leu Gly Glu Asp Asp Pro	240	245	250	255
Trp Leu Asp Asp Thr Ala Ala Trp Ile Glu Arg Ser Arg Gln Leu	260	265	270	275
Gln Lys Glu Lys Asp Leu Ala Glu Lys Arg Ala Lys Leu Leu Glu	280	285	290	295
Glu Met Asp Gln Glu Phe Gly Val Ser Thr Leu Val Glu Glu Glu	300	305	310	315
Phe Gly Gln Arg Arg Gln Asp Leu Tyr Ser Ala Arg Asp Leu Gln	320	325	330	335
Gly Leu Thr Val Glu His Ala Ile Asp Ser Phe Arg Glu Gly Glu	340	345	350	355
Thr Met Ile Leu Thr Leu Lys Asp Lys Gly Val Leu Gln Glu Glu				
Glu Asp Val Leu Val Asn Val Asn Leu Val Asp Lys Glu Arg Ala				
Glu Lys Asn Val Glu Leu Arg Lys Lys Lys Pro Asp Tyr Leu Pro				
Tyr Ala Glu Asp Glu Ser Val Asp Asp Leu Ala Gln Gln Lys Pro				
Arg Ser Ile Leu Ser Lys Tyr Asp Glu Glu Leu Gly Glu Arg				
Pro His Ser Phe Arg Leu Glu Gln Gly Gly Thr Ala Asp Gly Leu				

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Arg Glu Arg Glu Leu Glu Glu Ile Arg Ala Lys Leu Arg Leu Gln
 365 370 375
 Ala Gln Ser Leu Ser Thr Val Gly Pro Arg Leu Ala Ser Glu Tyr
 380 385 390
 Leu Thr Pro Glu Glu Met Val Thr Phe Lys Lys Thr Lys Arg Arg
 395 400 405
 Val Lys Lys Ile Arg Lys Lys Glu Lys Glu Val Val Val Arg Ala
 410 415 420
 Asp Asp Leu Leu Pro Leu Gly Asp Gln Thr Gln Asp Gly Asp Phe
 425 430 435
 Gly Ser Arg Leu Arg Gly Arg Gly Arg Arg Arg Val Ser Glu Val
 440 445 450
 Glu Glu Glu Lys Glu Pro Val Pro Gln Pro Leu Pro Ser Asp Asp
 455 460 465
 Thr Arg Val Glu Asn Met Asp Ile Ser Asp Glu Glu Glu Gly Gly
 470 475 480
 Ala Pro Pro Pro Ala Ser Pro Gln Val Leu Glu Glu Asp Glu Ala
 485 490 495
 Glu Leu Glu Leu Gln Lys Gln Leu Glu Lys Gly Arg Arg Leu Arg
 500 505 510
 Gln Leu Gln Gln Leu Gln Gln Leu Arg Asp Ser Gly Glu Lys Val
 515 520 525
 Val Glu Ile Val Lys Lys Leu Glu Ser Arg Gln Arg Gly Trp Glu
 530 535 540
 Glu Asp Glu Asp Pro Glu Arg Lys Gly Ala Ile Val Phe Asn Ala
 545 550 555
 Thr Ser Glu Phe Cys Arg Thr Leu Gly Glu Ile Pro Thr Tyr Gly
 560 565 570
 Leu Ala Gly Asn Arg Glu Glu Gln Glu Glu Leu Met Asp Phe Glu
 575 580 585
 Arg Asp Glu Glu Arg Ser Ala Asn Gly Gly Ser Glu Ser Asp Gly
 590 595 600
 Glu Glu Asn Ile Gly Trp Ser Thr Val Asn Leu Asp Glu Glu Lys
 605 610 615
 Gln Gln Gln Asp Phe Ser Ala Ser Ser Thr Thr Ile Leu Asp Glu
 620 625 630
 Glu Pro Ile Val Asn Arg Gly Leu Ala Ala Ala Leu Leu Leu Cys
 635 640 645
 Gln Asn Lys Gly Leu Leu Glu Thr Thr Val Gln Lys Val Ala Arg
 650 655 660
 Val Lys Ala Pro Asn Lys Ser Leu Pro Ser Ala Val Tyr Cys Ile
 665 670 675
 Glu Asp Lys Met Ala Ile Asp Asp Lys Tyr Ser Arg Arg Glu Glu
 680 685 690
 Tyr Arg Gly Phe Thr Gln Asp Phe Lys Glu Lys Asp Gly Tyr Lys
 695 700 705
 Pro Asp Val Lys Ile Glu Tyr Val Asp Glu Thr Gly Arg Lys Leu
 710 715 720
 Thr Pro Lys Glu Ala Phe Arg Gln Leu Ser His Arg Phe His Gly
 725 730 735
 Lys Gly Ser Gly Lys Met Lys Thr Glu Arg Arg Met Lys Lys Leu
 740 745 750
 Asp Glu Glu Ala Leu Leu Lys Lys Met Ser Ser Ser Asp Thr Pro
 755 760 765
 Leu Gly Thr Val Ala Leu Leu Gln Glu Lys Gln Lys Ala Gln Lys
 770 775 780
 Thr Pro Tyr Ile Val Leu Ser Gly Ser Gly Lys Ser Met Asn Ala
 785 790 795
 Asn Thr Ile Thr Lys
 800

<210> 52
 <211> 713
 <212> PRT

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<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5678487CD1

<400> 52

Met	Ala	Lys	Ser	Pro	Glu	Asn	Ser	Thr	Leu	Glu	Glu	Ile	Leu	Gly
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Gln	Tyr	Gln	Arg	Ser	Leu	Arg	Glu	His	Ala	Ser	Arg	Ser	Ile	His
				20					25					30
Gln	Leu	Thr	Cys	Ala	Leu	Lys	Glu	Gly	Asp	Val	Thr	Ile	Gly	Glu
				35					40					45
Asp	Ala	Pro	Asn	Leu	Ser	Phe	Ser	Thr	Ser	Val	Gly	Asn	Glu	Asp
				50					55					60
Ala	Arg	Thr	Ala	Trp	Pro	Glu	Leu	Gln	Gln	Ser	His	Ala	Val	Asn
				65					70					75
Gln	Leu	Lys	Asp	Leu	Leu	Arg	Gln	Gln	Ala	Asp	Lys	Glu	Ser	Glu
				80					85					90
Val	Ser	Pro	Ser	Arg	Arg	Arg	Lys	Met	Ser	Pro	Leu	Arg	Ser	Leu
				95					100					105
Glu	His	Glu	Glu	Thr	Asn	Met	Pro	Thr	Met	His	Asp	Leu	Val	His
				110					115					120
Thr	Ile	Asn	Asp	Gln	Ser	Gln	Tyr	Ile	His	His	Leu	Glu	Ala	Glu
				125					130					135
Val	Lys	Phe	Cys	Lys	Glu	Glu	Leu	Ser	Gly	Met	Lys	Asn	Lys	Ile
				140					145					150
Gln	Val	Val	Val	Leu	Glu	Asn	Glu	Gly	Leu	Gln	Gln	Gln	Leu	Lys
				155					160					165
Ser	Gln	Arg	Gln	Glu	Glu	Thr	Leu	Arg	Glu	Gln	Thr	Leu	Leu	Asp
				170					175					180
Ala	Ser	Gly	Asn	Met	His	Asn	Ser	Trp	Ile	Thr	Thr	Gly	Glu	Asp
				185					190					195
Ser	Gly	Val	Gly	Glu	Thr	Ser	Lys	Arg	Pro	Phe	Ser	His	Asp	Asn
				200					205					210
Ala	Asp	Phe	Gly	Lys	Ala	Ala	Ser	Ala	Gly	Glu	Gln	Leu	Glu	Leu
				215					220					225
Glu	Lys	Leu	Lys	Leu	Thr	Tyr	Glu	Glu	Lys	Cys	Glu	Ile	Glu	Glu
				230					235					240
Ser	Gln	Leu	Lys	Phe	Leu	Arg	Asn	Asp	Leu	Ala	Glu	Tyr	Gln	Arg
				245					250					255
Thr	Cys	Glu	Asp	Leu	Lys	Glu	Gln	Leu	Lys	His	Lys	Glu	Phe	Leu
				260					265					270
Leu	Ala	Ala	Asn	Thr	Cys	Asn	Arg	Val	Gly	Gly	Leu	Cys	Leu	Lys
				275					280					285
Cys	Ala	Gln	His	Glu	Ala	Val	Leu	Ser	Gln	Thr	His	Thr	Asn	Val
				290					295					300
His	Met	Gln	Thr	Ile	Glu	Arg	Leu	Val	Lys	Glu	Arg	Asp	Asp	Leu
				305					310					315
Met	Ser	Ala	Leu	Val	Ser	Val	Arg	Ser	Ser	Leu	Ala	Asp	Thr	Gln
				320					325					330
Gln	Arg	Glu	Ala	Ser	Ala	Tyr	Glu	Gln	Val	Lys	Gln	Val	Leu	Gln
				335					340					345
Ile	Ser	Glu	Glu	Ala	Asn	Phe	Glu	Lys	Thr	Lys	Ala	Leu	Ile	Gln
				350					355					360
Cys	Asp	Gln	Leu	Arg	Lys	Glu	Leu	Glu	Arg	Gln	Ala	Glu	Arg	Leu
				365					370					375
Glu	Lys	Asp	Leu	Ala	Ser	Gln	Gln	Glu	Lys	Arg	Ala	Ile	Glu	Lys
				380					385					390
Asp	Met	Met	Lys	Lys	Glu	Ile	Thr	Lys	Glu	Arg	Glu	Tyr	Met	Gly
				395					400					405
Ser	Lys	Met	Leu	Ile	Leu	Ser	Gln	Asn	Ile	Ala	Gln	Leu	Glu	Ala
				410					415					420

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Gln Val Glu Lys Val Thr Lys Glu Lys Ile Ser Ala Ile Asn Gln
 425 435
 Leu Glu Glu Ile Gln Ser Gln Leu Ala Ser Arg Glu Met Asp Val
 440 450
 Thr Lys Val Cys Gly Glu Met Arg Tyr Gln Leu Asn Lys Thr Asn
 455 465
 Met Glu Lys Asp Glu Ala Glu Lys Glu His Arg Glu Phe Arg Ala
 470 480
 Lys Thr Asn Arg Asp Leu Glu Ile Lys Asp Gln Glu Ile Glu Lys
 485 495
 Leu Arg Ile Glu Leu Asp Glu Ser Lys Gln His Leu Glu Gln Glu
 500 510
 Gln Gln Lys Ala Ala Leu Ala Arg Glu Glu Cys Leu Arg Leu Thr
 515 525
 Glu Leu Leu Gly Glu Ser Glu His Gln Leu His Leu Thr Arg Gln
 530 540
 Glu Lys Asp Ser Ile Gln Gln Ser Phe Ser Lys Glu Ala Lys Ala
 545 555
 Gln Ala Leu Gln Ala Gln Gln Arg Glu Gln Glu Leu Thr Gln Lys
 560 570
 Ile Gln Gln Met Glu Ala Gln His Asp Lys Thr Glu Asn Glu Gln
 575 585
 Tyr Leu Leu Leu Thr Ser Gln Asn Thr Phe Leu Thr Lys Leu Lys
 590 600
 Glu Glu Cys Cys Thr Leu Ala Lys Lys Leu Glu Gln Ile Ser Gln
 605 615
 Lys Thr Arg Ser Glu Ile Ala Gln Leu Ser Gln Glu Lys Arg Tyr
 620 630
 Thr Tyr Asp Lys Leu Gly Lys Leu Gln Arg Arg Asn Glu Glu Leu
 635 645
 Glu Glu Gln Cys Val Gln His Gly Arg Val His Glu Thr Met Lys
 650 660
 Gln Arg Leu Arg Gln Leu Asp Lys His Ser Gln Ala Thr Ala Gln
 665 675
 Gln Leu Val Gln Leu Leu Ser Lys Gln Asn Gln Leu Leu Leu Glu
 680 690
 Arg Gln Ser Leu Ser Glu Glu Val Asp Arg Leu Arg Thr Gln Leu
 695 705
 Pro Ser Met Pro Gln Ser Asp Cys
 710

<210> 53

<211> 880

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5682976CD1

<400> 53

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 20 25 30
 Tyr Leu Gly Arg Arg Glu Phe Ile Gln Arg Leu Lys Leu Glu Ala
 35 40 45
 Thr Leu Asn Val His Asp Gly Cys Val Asn Thr Ile Cys Trp Asn
 50 55 60
 Asp Thr Gly Glu Tyr Ile Leu Ser Gly Ser Asp Asp Thr Lys Leu
 65 70 75
 Val Ile Ser Asn Pro Tyr Ser Arg Lys Val Leu Thr Thr Ile Arg
 80 85 90
 Ser Gly His Arg Ala Asn Ile Phe Ser Ala Lys Phe Leu Pro Cys

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	95		100		105
Thr Asn Asp Lys	Gln	Ile Val Ser Cys	Gly Asp Gly Val	Ile	
	110				120
Phe Tyr Thr Asn	Val	Glu Gln Asp Ala	Thr Asn Arg Gln	Cys	
	125				135
Gln Phe Thr Cys	His	Tyr Gly Thr Thr	Glu Ile Met Thr	Val	
	140				150
Pro Asn Asp Pro	Tyr	Thr Phe Leu Ser	Cys Gly Glu Asp Gly	Thr	
	155				165
Val Arg Trp Phe	Asp	Thr Arg Ile Lys	Thr Ser Cys Thr Lys	Glu	
	170				180
Asp Cys Lys Asp	Asp	Ile Leu Ile Asn	Cys Arg Arg Ala Ala	Thr	
	185				195
Ser Val Ala Ile	Cys	Pro Pro Ile Pro	Tyr Tyr Leu Ala Val	Gly	
	200				210
Cys Ser Asp Ser	Ser	Val Arg Ile Tyr	Asp Arg Arg Met Leu	Gly	
	215				225
Thr Arg Ala Thr	Gly	Asn Tyr Ala Gly	Arg Gly Thr Thr Gly	Met	
	230				240
Val Ala Arg Phe	Ile	Pro Ser His Leu	Asn Asn Lys Ser Cys	Arg	
	245				255
Val Thr Ser Leu	Cys	Tyr Ser Glu Asp	Gly Gln Glu Ile Leu	Val	
	260				270
Ser Tyr Ser Ser	Asp	Tyr Ile Tyr Leu	Phe Asp Pro Lys Asp	Asp	
	275				285
Thr Ala Arg Glu	Leu	Lys Thr Pro Ser	Ala Glu Glu Arg Asp	Glu	
	290				300
Glu Leu Arg Gln	Pro	Pro Val Lys Arg	Leu Arg Leu Arg Gly	Asp	
	305				315
Trp Ser Asp Thr	Gly	Pro Arg Ala Arg	Pro Glu Ser Glu Arg	Glu	
	320				330
Arg Asp Gly Glu	Gln	Ser Pro Asn Val	Ser Leu Met Gln Arg	Met	
	335				345
Ser Asp Met Leu	Ser	Arg Trp Phe Glu	Glu Ala Ser Glu Val	Ala	
	350				360
Gln Ser Asn Arg	Gly	Arg Gly Arg Ser	Arg Pro Arg Gly Gly	Thr	
	365				375
Ser Gln Ser Asp	Ile	Ser Thr Leu Pro	Thr Val Pro Ser Ser	Pro	
	380				390
Asp Leu Glu Val	Ser	Glu Thr Ala Met	Glu Val Asp Thr Pro	Ala	
	395				405
Glu Gln Phe Leu	Gln	Pro Ser Thr Ser	Ser Thr Met Ser Ala	Gln	
	410				420
Ala His Ser Thr	Ser	Ser Pro Thr Glu	Ser Pro His Ser Thr	Pro	
	425				435
Leu Leu Ser Ser	Pro	Asp Ser Glu Gln	Arg Gln Ser Val Glu	Ala	
	440				450
Ser Gly His His	Thr	His His Gln Ser	Asp Ser Pro Ser Ser	Val	
	455				465
Val Asn Lys Gln	Leu	Gly Ser Met Ser	Leu Asp Glu Gln Gln	Asp	
	470				480
Asn Asn Asn Glu	Lys	Leu Ser Pro Lys	Pro Gly Thr Gly Glu	Pro	
	485				495
Val Leu Ser Leu	His	Tyr Ser Thr Glu	Gly Thr Thr Thr Ser	Thr	
	500				510
Ile Lys Leu Asn	Phe	Thr Asp Glu Trp	Ser Ser Ile Ala Ser	Ser	
	515				525
Ser Arg Gly Ile	Gly	Ser His Cys Lys	Ser Glu Gly Gln Glu	Glu	
	530				540
Ser Phe Val Pro	Gln	Ser Ser Val Gln	Pro Pro Glu Gly Asp	Ser	
	545				555
Glu Thr Lys Ala	Pro	Glu Glu Ser Ser	Glu Asp Val Thr Lys	Tyr	
	560				570

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Gln Glu Gly Val Ser Ala Glu Asn Pro Val Glu Asn His Ile Asn 585
 575
 Ile Thr Gln Ser Asp Lys Phe Thr Ala Lys Pro Leu Asp Ser Asn 585
 590
 Ser Gly Glu Arg Asn Asp Leu Asn Leu Asp Arg Ser Cys Gly Val 600
 605
 Pro Glu Glu Ser Ala Ser Ser Glu Lys Ala Lys Glu Pro Glu Thr 615
 620
 Ser Asp Gln Thr Ser Thr Glu Ser Ala Thr Asn Glu Asn Asn Thr 630
 635
 Asn Pro Glu Pro Gln Phe Gln Thr Glu Ala Thr Gly Pro Ser Ala 645
 650
 His Glu Glu Thr Ser Thr Arg Asp Ser Ala Leu Gln Asp Thr Asp 660
 665
 Asp Ser Asp Asp Asp Pro Val Leu Ile Pro Gly Ala Arg Tyr Arg 675
 680
 Ala Gly Pro Gly Asp Arg Arg Ser Ala Val Ala Arg Ile Gln Glu 690
 695
 Phe Phe Arg Arg Arg Lys Glu Arg Lys Glu Met Glu Glu Leu Asp 705
 710
 Thr Leu Asn Ile Arg Arg Pro Leu Val Lys Met Val Tyr Lys Gly 720
 725
 His Arg Asn Ser Arg Thr Met Ile Lys Glu Ala Asn Phe Trp Gly 735
 740
 Ala Asn Phe Val Met Ser Gly Ser Asp Cys Gly His Ile Phe Ile 750
 755
 Trp Asp Arg His Thr Ala Glu His Leu Met Leu Leu Glu Ala Asp 765
 770
 Asn His Val Val Asn Cys Leu Gln Pro His Pro Phe Asp Pro Ile 780
 785
 Leu Ala Ser Ser Gly Ile Asp Tyr Asp Ile Lys Ile Trp Ser Pro 810
 800
 Leu Glu Glu Ser Arg Ile Phe Asn Arg Lys Leu Ala Asp Glu Val 825
 815
 Ile Thr Arg Asn Glu Leu Met Leu Glu Glu Thr Arg Asn Thr Ile 840
 830
 Thr Val Pro Ala Ser Phe Met Leu Arg Met Leu Ala Ser Leu Asn 855
 845
 His Ile Arg Ala Asp Arg Leu Glu Gly Asp Arg Ser Glu Gly Ser 870
 860
 Gly Gln Glu Asn Glu Asn Glu Asp Glu Glu 880
 875

<210> 54

<211> 855

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5992432CD1

<400> 54

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 Val Phe Glu Glu Glu Asp Leu Pro Tyr Glu Glu Glu Ile Met Arg
 20 25 30
 Asn Gln Phe Ser Val Lys Cys Trp Leu Arg Tyr Ile Glu Phe Lys
 35 40 45
 Gln Gly Ala Pro Lys Pro Arg Leu Asn Gln Leu Tyr Glu Arg Ala
 50 55 60
 Leu Lys Leu Leu Pro Cys Ser Tyr Lys Leu Trp Tyr Arg Tyr Leu
 65 70 75
 Lys Ala Arg Arg Ala Gln Val Lys His Arg Cys Val Thr Asp Pro

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Ala Tyr Glu Asp Val	80	Asn Asn Cys His	85	Glu Arg Ala Phe Val	90
Met His Lys Met Pro	95	Arg Leu Trp Leu	100	Tyr Cys Gln Phe Leu	105
Met Asp Gln Gly Arg	110	Val Thr His Thr	115	Arg Thr Phe Asp Arg	120
Ala Leu Arg Ala Leu	125	Pro Ile Thr Gln	130	Ser Arg Ile Trp Pro	135
Leu Tyr Leu Arg Phe	140	Leu Arg Ser His	145	Pro Leu Pro Glu Thr	150
Val Arg Gly Tyr Arg	155	Arg Phe Leu Lys	160	Ser Pro Glu Ser	165
Glu Glu Tyr Ile Glu	170	Tyr Leu Lys Ser	175	Asp Arg Leu Asp	180
Ala Ala Gln Arg Leu	185	Ala Thr Val Val	190	Asp Glu Arg Phe	195
Ser Lys Ala Gly Lys	200	Ser Asn Tyr Gln	205	Trp His Glu Leu	210
Asp Leu Ile Ser Gln	215	Asn Pro Asp Lys	220	Val Gln Ser Leu	225
Asp Ala Ile Ile Arg	230	Gly Gly Leu Thr	235	Arg Phe Thr Asp	240
Gly Lys Leu Trp Cys	245	Ser Leu Ala Asp	250	Tyr Tyr Ile Arg	255
His Phe Glu Lys Ala	260	Arg Asp Val Tyr	265	Glu Ala Ile Arg	270
Val Met Thr Val Arg	275	Asp Phe Thr Gln	280	Val Phe Asp Ser	285
Gln Phe Glu Glu Ser	290	Met Ile Ala Ala	295	Met Glu Thr Ala	300
Glu Leu Gly Arg Glu	305	Glu Glu Asp Asp	310	Val Asp Leu Glu	315
Leu Ala Arg Phe Glu	320	Gln Leu Ile Ser	325	Arg Pro Leu Leu	330
Asn Ser Val Leu Leu	335	Arg Gln Asn Pro	340	His Val His Glu	345
His Lys Arg Val Ala	350	Leu His Gln Gly	355	Pro Arg Glu Ile	360
Asn Thr Tyr Thr Glu	365	Ala Val Gln Thr	370	Val Asp Pro Phe	375
Thr Gly Lys Pro His	380	Thr Leu Trp Val	385	Ala Phe Ala Lys	390
Glu Asp Asn Gly Gln	395	Leu Asp Asp Ala	400	Val Ile Leu Glu	405
Ala Thr Lys Val Asn	410	Phe Lys Gln Val	415	Asp Asp Leu Ala	420
Trp Cys Gln Cys Gly	425	Glu Leu Glu Leu	430	Arg His Glu Asn	435
Glu Ala Leu Arg Leu	440	Leu Arg Lys Ala	445	Thr Ala Leu Pro	450
Arg Ala Glu Tyr Phe	455	Asp Gly Ser Glu	460	Pro Val Gln Asn	465
Tyr Lys Ser Leu Lys	470	Val Trp Ser Met	475	Leu Ala Asp Leu	480
Ser Leu Gly Thr Phe	485	Gln Ser Thr Lys	490	Ala Val Tyr Asp	495
Leu Asp Leu Arg Ile	500	Ala Thr Pro Gln	505	Val Ile Asn Tyr	510
Met Phe Leu Glu Glu	515	His Lys Tyr Phe	520	Glu Ser Phe Lys	525
Tyr Glu Arg Gly Ile	530	Ser Leu Phe Lys	535	Trp Pro Asn Val	540
	545		550	Ser Asp	555

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Ile Trp Ser Thr Tyr Leu Thr Lys Phe Ile Ala Arg Tyr Gly Gly
560 565
Arg Lys Leu Glu Arg Ala Arg Asp Leu Phe Glu Gln Ala Leu Asp
575 580
Gly Cys Pro Pro Lys Tyr Ala Lys Thr Leu Tyr Leu Leu Tyr Ala
590 595
Gln Leu Glu Glu Glu Trp Gly Leu Ala Arg His Ala Met Ala Val
605 610
Tyr Glu Arg Ala Thr Arg Ala Val Glu Pro Ala Gln Gln Tyr Asp
620 625
Met Phe Asn Ile Tyr Ile Lys Arg Ala Ala Glu Ile Tyr Gly Val
635 640
Thr His Thr Arg Gly Ile Tyr Gln Lys Ala Ile Glu Val Leu Ser
650 655
Asp Glu His Ala Arg Glu Met Cys Leu Arg Phe Ala Asp Met Glu
665 670
Cys Lys Leu Gly Glu Ile Asp Arg Ala Arg Ala Ile Tyr Ser Phe
680 685
Cys Ser Gln Ile Cys Asp Pro Arg Thr Thr Gly Ala Phe Trp Gln
695 700
Thr Trp Lys Asp Phe Glu Val Arg His Gly Asn Glu Asp Thr Ile
710 715
Lys Glu Met Leu Arg Ile Arg Arg Ser Val Gln Ala Thr Tyr Asn
725 730
Thr Gln Val Asn Phe Met Ala Ser Gln Met Leu Lys Val Ser Gly
740 745
Ser Ala Thr Gly Thr Val Ser Asp Leu Ala Pro Gly Gln Ser Gly
755 760
Met Asp Asp Met Lys Leu Leu Glu Gln Arg Ala Glu Gln Leu Ala
770 775
Ala Glu Ala Glu Arg Asp Gln Pro Leu Arg Ala Gln Ser Lys Ile
785 790
Leu Phe Val Arg Ser Asp Ala Ser Arg Glu Glu Leu Ala Glu Leu
800 805
Ala Gln Gln Val Asn Pro Glu Glu Ile Gln Leu Gly Glu Asp Glu
815 820
Asp Glu Asp Glu Met Asp Leu Glu Pro Asn Glu Val Arg Leu Glu
830 835
Gln Gln Ser Val Pro Ala Ala Val Phe Gly Ser Leu Lys Glu Asp
845 850

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<210> 55

<211> 1598

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 116462CB1

<400> 55

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ttagaatggt aacttgcccc ttgctcactc catgcttgcc ttggggaacc ggtgagaaac 120
tgcaatccat tggcggtagg aaccacgatt ccggcattc ccagtctcc gagtctctcg 180
ggcttccctt tccgggtctc gaggctgctg aaaccgaaac cgctgtgctg tgggcgcagc 240
gccgagattg attcaccctc acctgtgctg cactccagct gaccgaagta ggaagccaga 300
cgagctgtaa aacatgaacg gaagagtggg ttatttgctc actgaggaag agatcaatct 360
taccagaggg ccttcagggc tgggcttcaa catcgctcgg ggacagatc agcagtatgt 420
ctccaacgac agtggcatct acgtcagccg catcaaagaa aatggggctg cggccctgga 480
tggcgcgctc caggagggtg ataagatcct ttcggtaaat gcccaagacc taagaacct 540
gctgcaccag gatgctgtag acctctttcg taatgcaggc tatgctgtgt ccttgagagt 600
gcagcacagg ttacagggtg agaattggac tataggcat cgaggtgaag gggaccacag 660
tggattatccc atatttatgg tgctggtgcc agtgtttgcc ctcaaccatgg tagcagcctg 720

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ggctttcatg agataccggc aacaactttg aaaaacttgc tctctttcaa tactcccaat 780
gaagatacat ttcaactacc ctccaccctt gctattctgc catgtctttc cctctctctg 840
catagccaga tttaagatga ctgataccca ccccaaacct tgcgtgtcac agtctccaat 900
tcttcatatt ctaatgggaa agtaaaggta ttgtttgaag gaaaactgaa gaaaagactt 960
ggcttagaac aaatgaggag ttatatattt tactaggact ttgtatagaa attcagctac 1020
aacccaagaa gagaaagatt gagtcttctt gtcaccatag gcaatacctt tttctttagc 1080
tggtcatgca taaaggccag ctatgtgata tttagggaag aaaggatttt tctttttaat 1140
gatcttctct gggaaattat tgtggccttt atttaatttc taactacgta cctgggtgac 1200
tatatcgaca aagatgtgaa agagcatttt tactttttta aaaaaggcaa taacatata 1260
cacatacgta tgcaaatatt atagtataat atggagaaat atggagaatt taccatgaga 1320
aagctacttt gtggtgtcta ggtttctgat aaaaagggat atcttaactg aagaatttaa 1380
agagatactt aaacagagca aatgtagtag gaacaaggga gtgagcctta taagaggacg 1440
ttcagttctc tttattaaaa taataactga gactgggaga ggtggcctat gcctgtaaat 1500
cccagcattt tggtagcctg aagtgggaga ttgcttgagt ccaggagacc agcctgggca 1560
acatagcaaa acctcatctc tttttaaaaa aaaaaaaa 1598

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<210> 56

<211> 1432

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1210462CB1

<400> 56

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ctgacccagg tgaaaagcaa atcagagggg aagcttgcaa aacagattgt caaagtgtgt 180
ttggatcatt ttgaaaaaca gtattccaaa gaactcggag atgcctggaa tacagatagg 240
gagatactaa catctccatc atgctggcaa tatgctgtcc tgccttaaccg attcaattat 300
ctctttgaa tggaaggaa ttacatttgg aagggtctac acacactctc tcagggtatc 360
ttacccaact atcttaaatc agtgaagtgt taccttagca gaactccggg ccgaatccct 420
tcagaagaag accaaattgg aaacctgaaa aaatatatc tcttaaatgc tgcctctctt 480
ctcccagttg tggctctgga attaagggat ggggagaagg ttctggatct ctgtgctgct 540
cctggaggaa aatcaatagc tctgctgcag tgtgcttgtc caggttatct tcattgtaat 600
gaatatgata gctcgagatt gagggtggcta aggcagacgt tggaaatctt catcccaacg 660
cctttgataa atgtaattaa agtgtctgaa ttggatggca gaaaatggg agatgcacag 720
cctgaaatgt ttgacaaggt gttagttggat gctcctgtgt caaatgatcg aaagctgtgt 780
ttttctctct acctccagaa ggcctcctgt aggataagtc aaaggaggaa ttgctctctt 840
ctacagatag agctgttaag gctctgcaatt aaggccttac gtccctggagg gatccttgta 900
tactctacat gcaagctttc caaggcagaa aatcaagat gtatcagta aatttttaaac 960
tcccacggta acatcatgcc tatggacatt aaaggaatag caaggactgt ctcccacgac 1020
ttccacattt cctcccactg ccaggaaatgt gggctcttag tgattccaga taaggggcaa 1080
gcttgggggc caatgtatgt agccaaattg aagaaatcat ggagcacagg aaaaattggt 1140
catgaatttt taaactgtgt ttatgtgtta ttatatattt atttctgaac tcagtagcatg 1200
ttaattttta aataatttat cagtaaacctt ctctgggtct gtttggaaat ctattttagt 1260
aatactttag catcttagaa tctaggctgt agaatgttct aggtgtattt ttttccaga 1320
aataatctct taacaatgat ttaaggtggt cgagatgggt ttgttctcat attataaac 1380
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<210> 57

<211> 2317

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1305252CB1

<400> 57

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cacaaataaa cccctggacc ccttgtttcc ctacgtctta agggccgcga tgttgtacct 120

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agaagactat ctggaaatga ttgagcagct tccatggat ctgccccgacc gcttcacgga 180
aatgcccggag atggacctgc aggtgacagaa tgcattggat caactagaac aaagaagtcag 240
tgaattcttt atgaatgcaa agaaaaataa acctgagtggt agggaaagacg aaatggcacc 300
catcaaaaaa gactactata aagcttttga agatgcagat gagaaggttc agttggcaaa 360
ccagatataat gacttggtag atcgacactt gagaagactg gatcagaacg tggctaaagtt 420
taaaatggag ctggaagctg ataattgctg aattacagaa atcttagaga gcgcatcttt 480
ggaattagac actccttcac agccagtgaa caatcaccat gctcattcac atactccagt 540
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<223> Incyte ID No: 1416289CB1

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<212> DNA

<213> Homo sapiens

<220>

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<223> Incyte ID No: 1752768CB1

<400> 61

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<210> 62

<211> 1865

<212> DNA

<213> Homo sapiens

<220>

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 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 2049176CB1

<400> 64
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 catattatgc atacaaagct gtgaaaaaca aaaaacgtga ggaatatggt cgaatggatg 180
 tgtactggat tgtttttgct ctctataact tgattgaaac agtagccgat caaacagttg 240
 cttggtttcc cttgttactat gagctgaaga ttgctttttg catatggctgt cttctccctt 300
 ataccaaagg agcaagttaa atatatagaa aatcctctca tccacttctt tcttcaaaag 360
 aaagggagat tgatgattat attgtacaag caaagggaac aggctatgaa accatggtta 420

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actttggcagc gcaagggttta aaccttgcag ctactgctgc tgttactgca gcagtaaaga 480
gccaaaggagc aataaactgaa cgtttaagaa gcttcagtat gcatgattta acaactatcc 540
aagggtgatga gccctgtggga caaagaccat accaaccctc accagaagca aaaaagaaaa 600
gtaaaccagc ccccgctgaa tcagcaggtt atggaattcc accgtaaaag ggagatgaga 660
aaacagatga agaagcagag gggccatatt catgataatga gatgttaaca cacaaggagg 720
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gtcaaatatc ccaagacaga ttatgctaaa tacatgcact tcactctcta acatgatata 900
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<210> 65
<211> 2035
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2686765CB1

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<400> 65
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gcgcaagagc gacaagtatg gcttcccttg gggcagccag tactcgggca gcttagagag 480
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<210> 66
<211> 766
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3215187CB1

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<400> 66
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tctctgggtgc tgtgcgctgc gctcatcttc ttgccactct ggcacataat tgcctttgat 180
gagtttaagga cagatttttaa gagccccata gaccagtgca atcctgttca tgcgaggggaa 240
cggttgagga acatcgagcg catctgcttc ctctcgcaa agctgggtct gccagaatac 300
tccatccata gcctctctctg cattatgttc ctgtgtgcgc aagagtgtct cagctggggg 360
ctgaatgtcc ctctactttt ctatcacttc tggaggtatt tccactgtcc accgatagc 420
tcagaactag cctacgacccc accgggtgttc atgaatgccg acacttttag ttactgtcag 480
aaggagcgct ggtcttaagct ggccttctat ctccctctct tcttcaata cctttactgc 540
atgatctaca cttttagtgag ctcttaacgc aaagaccatg cacatcatca gagactgaga 600
tgggagaggg ctgagacgga gaggtgcatt tctgtgtgtg actggaggag ggaaccagaat 660
gaggatagct gagatataga cccggcagcg agtcagactg aatgggagct ggaatcacgc 720
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<210> 67
<211> 2503
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3500375CB1

<400> 67
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caagagaaga aggaggcagg cgccgcgcca gccgcccgcg cccgagccgg cggaggcgag 180
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agggatgtga ctattttgaa tgaatcagaa tgtcaacttg tatgtacact atatctcac 2220

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ttactcatta tttaaaaaga ataataaaaa atctagatca attcttcaat ttgattgaac 2340
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cttctcactg acttttggtga ttttgaaacc tagaatgatg tgtttctatc tgtaatatct 2460
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<210> 68
<211> 541
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte ID No: 5080410CB1

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<400> 68
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atcgtctctc gcttccatgg cctctcgctc gcagtgaagc tcaagttgct actcgggagc 180
ctgcacctcc cgcccgccac ggtggacgag catctattt tgccaaatga gggcgcccta 240
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atgctgccac tggagtcca gtacttgaac aaaaacggcg ctgacgaccc tcgcgggacc 480
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<210> 69
<211> 937
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte ID No: 5218248CB1

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<400> 69
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gagaaacacc tgttcaacct gaagtctcgc gccaaagaa tgagttaggag tgccaaaaaa 180
tgcgataagg aggaaaaggc cgaaaaggcc aaaattaaaa aggccattca gaagggcaac 240
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caggtatgaac tgtctcagag actggcccgc ctccgggac aagtgtgacg gcagaacccg 720
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tataccctag aaactctgaa cagcccgaaa tgcgtgaaat cccttctac tttgggttta 840
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<210> 70
<211> 823
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte ID No: 058336CB1

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<400> 70

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tcccgggtgcg agaagaagac cccggcttga gagtgcgatg cggtttaatg attgcttcag 180
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ttaacaattt accaaagaga tattgatatt gaaggaaatt gggaggagga aaagaaacct 720
ggggtgaata cttattttca gtgcatcatt actgttcagg attcctatga tggatggcag 780
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<210> 71

<211> 1033

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1511488CB1

<400> 71

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acaagcggcg agcatgctca gggcggtcgg gagcctaact cgccttgacc gcgggctaac 180
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<210> 72

<211> 1622

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1638819CB1

<400> 72

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gtgtacgtga ctgaccggag aacctcacag agaactctcg aggtgcttcc tggcaggaga 480
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<210> 73

<211> 2449

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1655123CB1

<400> 73

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<210> 74
<211> 1689
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2553926CB1

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<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 2800717CB1

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<210> 76

<211> 898

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5664154CB1

<400> 76

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gctcattata tattgtgaag ttaataaaaa agttttaaaa agcaaaaaaa aaaaaaaa 898

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 <211> 1236
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 017900CB1

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 <211> 1634
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<220>
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<211> 1258
<212> DNA
<213> Homo sapiens

<220>
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<223> Incyte ID No: 259983CB1

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<212> DNA
<213> Homo sapiens

<220>
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<210> 81

<211> 1370

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 1398816CB1

<400> 81

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<223> Incyte ID No: 1496820CB1

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 <213> Homo sapiens

<220>
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2555

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<213> Homo sapiens

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<223> Incyte ID No: 1980010CB1

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<222> 2058, 2067

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<223> Incyte ID No: 2683225CB1

<400> 96

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<210> 99

<211> 1889

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 3082014CB1

<220>

<221> unsure

<222> 1809, 1848, 1853, 1880

<223> a, t, c, g, or other

<400> 99

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<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte ID No: 3520701CB1

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<210> 101

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 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 4184320CB1

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<210> 102
 <211> 580
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> Incyte ID No: 4764233CB1

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<210> 103
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<220>
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 <223> Incyte ID No: 4817352CB1

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<211> 2257
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte ID No: 5040573CB1

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<210> 105

<211> 2550

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 5627029CB1

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WO 01/07471

PCT/US00/19948

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